McKnight Brain Research Foundation
Orientation Manual

April 2025

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This document represents a condensed summary of information relevant to the development and advancement of the programs of the MBRF in support of its Mission…

"To enhance life by preserving memory and supporting healthy cognitive aging through research and education."

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Evelyn Franks McKnight

Founder and Benefactor of the McKnight Brain Research Foundation

November 10, 1914 – October 2, 1999

…A brief biography

Evelyn Franks McKnight, daughter of Arthur and Bertha Franks of Connellsville, Pennsylvania, blazed a trail of recognition and accomplishments throughout her life from November 10, 1914, to October 2, 1999. Following high school, she studied to become a nurse. Evelyn's mother, a seamstress, supplied the financial support for her daughter's nursing education. After leaving Connellsville, she launched her career as a registered nurse. For six years prior to Evelyn's emigration to Florida in 1946, she was employed in the Congress of the United States as a licensed nurse in the District of Colombia. During the Korean War she worked as a Captain in the United States Air Force at the Pentagon.

After her retirement from the Air Force, Evelyn returned to Miami, Florida, where she worked in the personnel section of the Trans World Airlines (TWA), followed by her employment as a staff nurse at the Miami Veterans Administration Medical Center (VAMC). Evelyn retired from the VAMC in 1965 and joined the registry for private duty nursing. She met William L. McKnight when she worked as his nurse. They were married in 1974 after the death of his first wife in 1973.

William McKnight was with the 3M Company for 59 years prior to his retirement in 1966 as President and Chairman of the Board. A multimillionaire industrialist and philanthropist, Mr. McKnight owned a large home on La Gorce Island, Miami Beach, Florida, and had many business interests in the Miami-Dade County area. He owned the Hialeah Park for horse racing and was chairman of the board of Miami's Calder Race Course and Tropical Park. Mr. McKnight also owned the popular and upscale Tony Sweet's Restaurant. He was a founding member and chairman of the board of the Surf Club, a very prestigious social club on Miami Beach, Florida.

The McKnights, together, were very interested in the philanthropic causes he had pursued through his previously established McKnight Foundation. These focused primarily on human services related to physical and social problems, grants for health and medical research, education plus the visual and performing arts. The McKnights' interest in the nervous system and the relationship between the eye and brain inspired their gift to the Bascom Palmer Eye Institute at the University of Miami to establish the William. L. McKnight Vision Research Center. They are among the largest contributors to the Bascom Palmer Eye Institute and the University of Miami.

During their marriage, William and Evelyn McKnight were favorite guests at many social functions. Often, upon leaving a social gathering, William would say to Evelyn…"Why is it I can't remember that person's name until after I've just left them?" As a result, and with Evelyn's background as a nurse, they became very interested in supporting research in memory loss related to the aging process. Prior to William's death in 1978, he and Evelyn would drive around Dade County on Sunday afternoons looking for property to build a brain institute to support research in cognitive decline and memory loss associated with the aging process.

Over the two decades after Mr. McKnight's death, Evelyn quietly oversaw and remained interested in and dedicated to maintaining the legacy of Mr. McKnight in both his business and philanthropic interests. As a result, on April 28, 1999, she established the McKnight Brain Research Foundation to support research of the brain to accomplish alleviation of memory loss of the aging as a legacy to her deceased husband.

Before Mrs. McKnight could realize the value of her gift in advancing the understanding and alleviation of age-related memory loss, she died on October 2, 1999. She will always be remembered as a gracious and gentle lady who accomplished great things and made a difference in the lives of many.

McKnight Brain Research Foundation (MBRF)

Vision, Value Statement, and Mission

Vision:

To: "Improve the quality of life through the understanding and alleviation of age-related memory loss."

Value Statement:

- ***Commitment***

  The MBRF is committed to its vision to understand and alleviate age-related memory loss, and expects the same of its grant recipients and research partners.

- ***Discovery***

  The MBRF values scientific curiosity and discovery leading to clinical intervention in age-related memory loss.

- ***Honesty/Integrity***

  The MBRF conducts its affairs with the highest degree of honesty, integrity, and accountability and expects the same of others.

Mission:

Lead in generating interest and support of scientific research to understand and alleviate age-related memory loss.

Inspire commitment and shared vision in the understanding and alleviation of age-related memory loss.

Nurture scientists dedicated to the exploration of innovative research initiatives intended for clinical application in age-related memory loss.

Promote collaboration and communication among research scientists, institutions, and organizations engaged in research in age-related memory loss.

Partner with research scientists, institutions, and organizations to promote research to understand and alleviate age-related memory loss.

Recognize and Reward significant achievement in discoveries leading to clinical intervention to understand and alleviate age-related memory loss.

Vision, Value Statement, Mission Adopted May 18, 2005
Reaffirmed July 22, 2020

McKNIGHT BRAIN
RESEARCH FOUNDATION
Preserving memory, enhancing life

STRATEGIC PLAN

2024 - 2026

Approved by Board of Trustees on October 23, 2023
Tentative Revision September 19, 2024

McKNIGHT BRAIN RESEARCH FOUNDATION
Preserving memory, enhancing life

STRATEGIC PLAN

2024 - 2026

The McKnight Brain Research Foundation initiates this strategic plan reflective of critical priorities and strategies to advance its purpose, position, and operations. This strategic plan's content is derived from a comprehensive analysis of the Foundation and the input of its Trustees and stakeholders. This plan is a 'living' document that can be updated and revised as it is implemented.

The duration of this strategic plan spans January 1, 2024 to December 31, 2026.

For the purpose of this strategic plan, the McKnight Brain Research Foundation defines cognitive aging as follows: Although cognition is sometimes equated with memory, cognition is multidimensional because it involves a number of interrelated abilities that depend on brain anatomy and physiology. Distinguishing among those component abilities is important since they play different roles in the processing of information and behavior and are differently impacted by aging. A conceptual definition of cognitive aging is a process of gradual, ongoing, yet highly variable changes in cognitive functions that occur as people get older. Cognitive aging is a lifelong process. It is not a disease or a quantifiable level of function.*

(*Source: National Academies of Sciences, Engineering, and Medicine. 2015. *Cognitive Aging: Progress in Understanding and Opportunities for Action*. Washington, DC: The National Academies Press.)

MISSION STATEMENT
To enhance life by preserving memory and supporting healthy cognitive aging through research and education

VISION STATEMENT
A healthy brain throughout life

CORE VALUES
Integrity – Commitment – Discovery – Collaboration – Inspiration – Inclusion

GOALS	OBJECTIVES
	Invest in and promote research focused on healthy cognitive aging
Advance research and scientific knowledge associated with age-related cognitive decline and memory loss	Place understanding about the naturally aging brain and optimal cognition at the forefront of public awareness
Educate the public and healthcare professionals about age-related cognitive decline and memory loss	Position the Foundation as the thought leader, research catalyst, and resource in age-related cognitive decline and memory loss
	Ensure the organizational structure, resources, and capacity to operate, advance, and sustain the Foundation and its mission

OBJECTIVE: Invest in and promote research focused on healthy cognitive aging

STRATEGIES	SUCCESS MEASURE	TIME FRAME	RESPONSIBILITY	PROGRESS
Identify research gaps in healthy cognitive aging and direct funding to support associated research	Designated and funded research priorities through strategic partnerships	2024 - 2026	Research Committee	
Increase number of research applicants and grantees focused on the application of research in healthy cognitive aging beyond the McKnight Brain Institutes	Number, diversity, and impact of funded applications beyond the McKnight Brain Institutes	2024 - 2026	Research Committee / Chief Executive Officer	
Evaluate McKnight Brain Institutes individually and collectively to ensure advancement of Foundation's mission and defined metrics	Quantified impact of McKnight Brain Institute investment Uniformity of McKnight Brain Institute reporting	Metrics & Uniformity Reporting 2024 Quantified Impact 2024 - 2026	Board / Research Committees / External Reviewers	
Define and improve collaborative research and coordination across McKnight Brain Institutes	Frequency and amount of collaborative work among McKnight Brain Institute leaders and researchers	Definition 2024 Improvement 2025 - 2026	McKnight Brain Institute Leadership Council / Board Chair	
Increase research dissemination beyond research and academic communities	Frequency, amount, and impact of research dissemination within the public arena	2024 - 2026	Communications Working Group / BRG Communications	

OBJECTIVE: Place education about the naturally aging brain and optimal cognition at the forefront of public awareness				
STRATEGIES	**SUCCESS MEASURE**	**TIME FRAME**	**RESPONSIBILITY**	**PROGRESS**
Develop and launch a comprehensive campaign that demonstrates what normal brain aging is and what to expect to reassure the public and mitigate fear	Number of media placements with message mentions on normal brain aging Audience engagement with online campaign tools and resources as measured by number of visited pages and downloaded resources	2024 - 2026	BRG Communications / Strategic Communications Consultant / Education Committee	
Act as a resource for healthcare professionals by equipping them with resources and information about cognitive aging and memory loss they can share with their patients	Number of resource materials delivered to the healthcare professional community and surrounding key audiences Number of thought leadership opportunities secured at healthcare professional focused conferences and events	2024 - 2026	BRG Communications / Strategic Communications Consultant / Chief Executive Officer	
Create a hub on the Foundation website to house resources for consumers and healthcare professionals, including	Number of resources downloaded from the hub	2024 - 2026	BRG Communications / Strategic Communications Consultant /	

campaign-specific tools and resources from other leading aging and brain health organizations	Number of other leading organizations featured on Foundation's website hub and reciprocal visibility		Chief Executive Officer / Education Committee	
Reach younger audiences (age 35 to 50) and engage them with campaign messages and tools where they consume related information	Number of impressions secured Number of media articles generated Social media reach and engagement, including increase in social media followers, likes, shares, and engagements with posts Increased web traffic Number of digital influencers engaged with campaign and reach of their audiences	2024 - 2026	BRG Communications / Strategic Communications Consultant / Education Committee	

OBJECTIVE: Position the Foundation as the thought leader, research catalyst, and resource in age-related cognitive decline and memory loss

STRATEGIES	SUCCESS MEASURE	TIME FRAME	RESPONSIBILITY	PROGRESS
Confirm and operationalize the definitions of cognitive aging, cognitive health, brain health, and related terms for public-facing messaging	Documented definitions approved by the Trustees	2024	Communications Committee / Education Committee / BRG Communications / Strategic Communications Consultant / Chief Executive Officer	
Reinforce the Foundation's position as leading research supporting organization on cognitive aging by leveraging the credibility and voice of its Trustees and McKnight Brain Institute experts	Foundation acknowledgement in funded and affiliated researchers' journal articles Number of experts quoted in media articles with Foundation recognition Number of speaking opportunities secured for the Foundation and McKnight Brain Institute experts	2024 - 2026	BRG Communications / Strategic Communications Consultant / Chief Executive Officer	

Be a convenor and collaborator with other leading aging and brain health organizations	Quality of strategic partnerships secured and activated Number of Foundation resources and information shared via partner channels and distribution networks Number of partner resources featured or shared on Foundation website hub and reciprocal visibility Improvement in Foundation's search ranking for relevant terms	2024 - 2026	BRG Communications / Chief Executive Officer / Board	
Build share of voice to reach audiences multiple times through a variety of mediums	Number of brand mentions in media placements Increase in share of voice as measured by percentage of articles on relevant topics that include the Foundation Number of Foundation and McKnight Brain Institute experts quoted in media placements	2024 - 2026	BRG Communications / Strategic Communications Consultant	

	Improvement in Foundation's search ranking for relevant terms			

OBJECTIVE: Ensure the organizational structure, resources, and capacity to operate, advance, and sustain the Foundation and its mission

STRATEGIES	SUCCESS MEASURE	TIME FRAME	RESPONSIBILITY	PROGRESS
Clarify and update board and staff roles, responsibilities, and functions	Trustee and staff roles and responsibilities aligned with function Leveraged Chief Executive Officer capacity	Completion 2024 Oversight Support 2025 - 2026	Board / Chief Executive Officer / Legal Counsel	
Review Foundation governance documents to ensure alignment with Foundation direction and requirements, updating as applicable	Up-to-date and relevant governance documents including as informed by determined role clarity	2024	Membership and Governance Committee	
Review, monitor, and build board membership to optimize Trustee diversity and skill sets	Documented and executed board membership recruitment plan Reviewed and monitored board diversity and skill sets	2024 - 2026	Membership and Governance Committee / Board	
Develop and implement board succession plan for Officers and Trustees based on governance best practice	Documented and executed plan for board officers' development and succession	2025	Membership and Governance Committee / Board	

	Documented and executed board membership recruitment plan			
Evaluate and secure a technology platform to track Foundation activities and metrics	Single operational database to document, track, and report performance to the Foundation	2024 - 2025	Chief Executive Officer / Corporate Trustee / Board	

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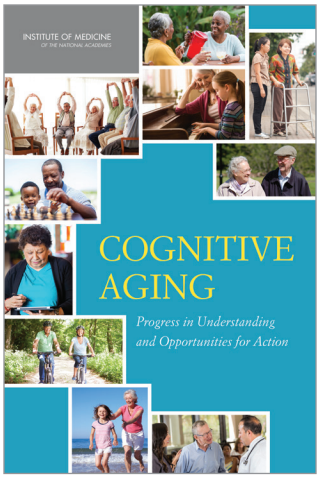
Cognitive Aging

Progress in Understanding and Opportunities for Action



For most Americans, staying "mentally sharp" as they age is a very high priority. Declines in memory and decision-making abilities may trigger fears of Alzheimer's disease or other neurodegenerative diseases. However, cognitive aging is a natural process that can have both positive and negative effects on cognitive function in older adults—effects that vary widely among individuals. At this point in time, when the older population is rapidly growing in the United States and across the globe, it is important to examine what is known about cognitive aging and to identify and promote actions that individuals, organizations, communities, and society can take to help older adults maintain and improve their cognitive health.

It is important to identify and promote actions that individuals, organizations, communities, and society can take to help older adults maintain and improve their cognitive health.

With support from the McKnight Brain Research Foundation, the National Institute on Aging, the National Institute of Neurological Disorders and Stroke, AARP, the Retirement Research Foundation, and the Centers for Disease Control and Prevention, the Institute of Medicine (IOM) convened a committee to examine the public health dimensions of cognitive aging. In *Cognitive Aging: Progress in Understanding and Opportunities for Action*, the committee assesses the state of knowledge about cognitive aging, including definitions and terminology, epidemiology and surveillance, prevention and intervention, education of health professionals, and public awareness and education.

What Is Cognitive Aging?

Like other organs, the human brain changes with age in both its physical structures and its ability to carry out various functions. The brain is responsible for cognition, a term that includes memory, decision making, processing speed, wisdom, and learning. As a person ages, these functions may change—a process called cognitive aging.

Cognitive aging is not a disease. Instead, it is a process that occurs in every individual, beginning at birth and continuing throughout the life span.

Cognitive changes are different for each person, and an individual's cognitive function may vary from one day to another. Wisdom and expertise can increase with age, while speed of processing, decision making, and some types of memory may decline. Cognitive aging may affect daily tasks such as paying bills, driving, following recipes, and adhering to medication schedules. It may challenge an older person's ability to live independently, pursue favorite activities, and maintain a sense of identity. But there are specific actions that individuals and their families can take to support their cognitive function. It is important to overcome stigma and misconceptions that may prevent older adults from seeking resources that can promote their cognitive health and overall quality of life.

Steps for Individuals to Reduce Risks for Cognitive Decline

Despite wide variation in cognitive function among individuals, the committee identifies three actions, supported by scientific evidence, that everyone can take to maintain their cognitive health and potentially reduce the effects of cognitive aging. Specifically, the committee recommends that individuals should

1. Be physically active.
2. Reduce and manage cardiovascular disease risk factors (including hypertension, diabetes, and smoking).
3. Regularly discuss and review health conditions and medications that might influence cognitive health with a health care professional.

The committee also identifies additional actions for which there is some scientific evidence to suggest positive effects on cognitive health:

- Be socially and intellectually engaged, and continually seek opportunities to learn.

Characterizing Cognitive Aging

Key Features

- Inherent in humans and animals as they age.
- Occurs across the spectrum of individuals as they age regardless of initial cognitive function.
- Highly dynamic process with variability within and between individuals.
- Includes some cognitive domains that may not change, may decline, or may actually improve with aging, and there is the potential for older adults to strengthen some cognitive abilities.
- Only now beginning to be understood biologically yet clearly involves structural and functional brain changes.
- Not a clinically-defined neurological or psychiatric disease such as Alzheimer's disease and does not inevitably lead to neuronal death and neurodegenerative dementia (such as Alzheimer's disease).

Risk and Protective Factors

- Health and environmental factors over the life span influence cognitive aging.
- Modifiable and non-modifiable factors include genetics, culture, education, medical comorbidities, acute illness, physical activity, and other health behaviors.
- Cognitive aging can be influenced by development beginning in utero, infancy, and childhood.

Assessment

- Cognitive aging is not easily defined by clear thresholds on cognitive tests since many factors—including culture, occupation, education, environmental context, and health variables (e.g., medications, delirium)—influence test performance and norms.
- For an individual, cognitive performance is best asessed at several points in time.

Impact on Daily Life

- Day-to-day functions, such as driving, making financial and health care decisions, and understanding instructions given by health care professionals, may be affected.
- Experience, expertise, and environmental support aids (e.g., lists) can help compensate for declines in cognition.
- The challenges of cognitive aging may be more apparent in environments that require individuals to engage in highly technical and fast-paced or timed tasks, situations that involve new learning, or stressful situations (i.e., emotional, physical, or health-related), and less apparent in highly familiar situations.

It is important to overcome stigma and misconceptions that may prevent older adults from seeking resources that can promote cognitive health and overall quality of life.

- Get adequate sleep and receive treatment for sleep disorders as needed.
- Take steps to avoid the risks of cognitive changes due to delirium if hospitalized.

Finally, individuals and families should be aware of the potential for financial fraud and abuse, impaired driving skills, and poor consumer decision making, and they should make health, finance, and consumer decisions based on reliable evidence from trusted sources.

Steps for Health Care Providers to Address Cognitive Aging

Individuals and families are turning to health care professionals in increasing numbers for information and advice about cognitive health. These professionals need to be fully informed and ready to respond to patient queries. However, although cognitive aging occurs in every individual (compared with about 11 to 14 percent of older Americans who experience Alzheimer's disease or other dementias), there is relatively little research or clinical guidance about risk and protective factors or interventions for non-disease age-related declines in cognition. As a result, many health care providers consider cognitive health counseling a challenge.

The committee recommends that health professional schools, professional societies, and public and private health care organizations develop and disseminate core competencies, curricula, and continuing education opportunities that focus on cognitive aging (as distinct from clinical syndromes and diseases). Furthermore, the committee stresses that cognitive health should be promoted during regular medical and wellness visits for people of all ages. Specifically, health care professionals should use patient visits to

- identify risk factors for cognitive decline and recommend steps to minimize risk;
- review patient medications, especially those known to affect cognition;
- provide patients and families with information about cognitive aging and actions that may maintain cognitive health or prevent decline; and
- encourage patients and family members to discuss concerns about cognitive health.

Community Support, Policy Change, and Private-Sector Business Involvement to Address Cognitive Aging

The effects of cognitive aging have widespread societal consequences and require action in many sectors. An array of public health and social services are available to assist older adults and their families, and communities across the country are working to improve quality of life for aging individuals, but many challenges remain. Opportunities for action include

- Collect and disseminate population-based data on cognitive aging.
- Develop an independent information gateway on cognitive aging as well as consumer-relevant criteria for evaluating cognition-related products.
- Involve the financial, transportation, and technology industries in developing and implementing products, services, and informational materials focused on (1) maintaining and assessing older adults' driving skills

and making family decisions about safe driving; (2) banking and financial decision vulnerabilities; and (3) technology opportunities to accommodate cognitive changes.

Public Education and Engagement

Promoting cognitive health for older adults requires clear and effective communication with the public. Messages should be accurate, up-to-date, and consistent; resonate with diverse groups within the U.S. population; and encourage behaviors that promote cognitive health. Differentiating cognitive aging from Alzheimer's disease and dementia will be a major challenge for public information campaigns. Although Alzheimer's disease and other neurodegenerative diseases are an important area of focus, the committee calls for more attention to the needs of the vast majority of the aging population whose change in cognitive function is not related to disease.

Conclusion

"Cognitive aging is not just an individual or a family or a health care system challenge," the committee writes, "it is an issue that affects the fabric of society and requires actions by many and varied stakeholders." *Cognitive Aging: Progress in Understanding and Opportunities for Action* offers clear steps that individuals, families, communities, health care providers and systems, financial organizations, community groups, public health agencies and others can take to promote cognitive health and help older adults live fuller and more independent lives. Ultimately, the report calls for a societal commitment to cognitive aging as a public health issue that requires prompt action across many sectors.

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500 Fifth Street, NW
Washington, DC 20001
TEL 202.334.2352
FAX 202.334.1412

www.iom.edu

Recommendations from Institute of Medicine Study on Cognitive Aging Release date, April 14
…Progress in Understanding and Opportunities for Action

Release date, April 14, 2015

Recommendation 1: ***Increase Research and Tools for Assessing Cognitive Aging and Cognitive Trajectories***

The National Institutes of Health, the Centers for Disease Control and Prevention, research foundations, academic research institutions, and private-sector companies should expand research on the trajectories of cognitive aging and improve the tools used to assess cognitive changes and their effects on daily function.

Specific needs include

- Studies using a range of assessments (e.g., neuronal injury biomarkers, neuroimaging, postmortem assessments of neuronal integrity) to explore the physiological and structural basis of cognitive aging;
- Non-human animal studies that examine the mechanisms and clinical correlates of cognitive aging and that are designed to inform human cognitive aging;
- Studies to examine the mechanisms underlying interventions that affect the cognitive trajectory;
- Studies to identify and validate novel tools and measures of function that capture the complexities of real-world tasks and are sensitive to early changes in cognition and function; and
- An update of the norms for cognitive function in older adults (including those in the most advanced age groups) to include the consideration of disease, literacy, language, racial and ethnic diversity , culture, and socioeconomic factors.

Recommendation 2: ***Collect and Disseminate Population-Based Data on Cognitive Aging***
The Centers for Disease Control and Prevention (CDC), state health agencies, and other relevant government agencies, as well as nonprofit organizations, research foundations, and academic research institutions, should strengthen efforts to collect and disseminate population-based data on cognitive aging. These efforts should identify the nature and extent of cognitive aging throughout the population, including high-risk and underserved populations, with the goal of informing the general public and improving relevant policies, programs and services.

Specifically, expanded cognitive aging data collection and dissemination efforts should include

- A focus on the cognitive health of older adults as separate from dementia or other clinical neurodegenerative diseases.
- The development of operational definitions of cognitive aging for use in research and public health surveillance and also the development of a process for periodic reexamination. Analyses of existing longitudinal datasets of older persons should be used to inform these efforts.
- Expanded data collection efforts and further analyses of representative surveys involving geographically diverse and high-risk populations. These efforts should include cognitive testing when standardized, feasible, and clinically credible and also self-reports of perceptions or concerns regarding cognitive aging, personal and social adaptations, and self-care and other management practices.
- Longitudinal assessments of changes in cognitive performance and risk behaviors in diverse populations.
- Inclusion of cognition-related questions in the core instrument of the Behavioral Risk Factor Surveillance System, rather than an optional module.
- Exploration of other available relevant data on cognitive health such as health insurance claims data, sales and marketing data for cognition-related products and treatments, data on financial and banking transactions as well as on financial fraud and scams, and data on automobile insurance claims.
- Active dissemination of data on cognitive aging in the population. An annual or biennial report to the U.S. public should be issued by the CDC or other federal agency on the nature and extent of cognitive aging in the U.S. population.

Recommendation 3: ***Take Actions to Reduce Risks of Cognitive Decline with Aging***
Individuals of all ages and their families should take actions to maintain and sustain their cognitive health, realizing that there is wide variability in cognitive health among individuals.

Specifically, individuals should:

- Be physically active.
- Reduce and manage cardiovascular disease risk factors (including hypertension, diabetes, smoking).
- Regularly discuss and review health conditions and medications that might influence cognitive health with a health care professional.
- Take additional actions that may promote cognitive health, including
  - Be socially and intellectually engaged, and engage in lifelong learning;
  - Get adequate sleep and receive treatment for sleep disorders if needed;
  - Take steps to avoid the risk of cognitive changes due to delirium if hospitalized; and
  - Carefully evaluate products advertised to consumers to improve cognitive health, such as medications, nutritionals, and cognitive training.

Recommendation 4: ***Increase Research on Risk and Protective Factors and Interventions to Promote Cognitive Health and Prevent or Reduce Cognitive Decline***
The National Institutes of Health, the Centers for Disease Control and Prevention, other relevant government agencies, nonprofit organizations, and research foundations should expand research on risk and protective factors for cognitive aging and on interventions aimed at preventing or reducing cognitive decline and maintaining cognitive health.

Research efforts should:

- Develop collaborative approaches between ongoing longitudinal studies across the life span that focus on cognitive aging outcomes in order to maximize the amount and comparability of data available on risk and protective factors.
- Examine risk factors and interventions in under-studied and vulnerable populations, including people 85 years and older and those with childhood or youth trauma or developmental
- delay, mental illness, learning disabilities, or genetic intellectual disabilities and spanning ethnic/cultural and socioeconomic groups.
- Conduct single- and multicomponent clinical trials of promising interventions to promote cognitive health and prevent cognitive decline, testing for both cognitive status and functional outcomes.
- Assess cognitive outcomes in clinical trials that target the reduction of cardiovascular and other risk factors likely related to cognitive health.
- Explore older adults' preferences and values regarding cognitive health and aging and regarding specific cognitive interventions and training modalities.
- Identify effective approaches to sustaining behavior changes that promote healthy cognition across the life span.

Recommendation 5: ***Ensure Appropriate Review, Policies, and Guidelines for Products That Affect Cognitive Function or Assert Claims Regarding Cognitive Health***

The Food and Drug Administration and the Federal Trade Commission, in conjunction with other relevant federal agencies and consumer organizations, should determine the appropriate regulatory review, policies, and guidelines for

- **over-the-counter medications (such as antihistamines, sedatives, and other medications that have strong anticholinergic activity) that may affect cognitive function, and**
- **interventions (such as cognitive training, nutriceuticals, supplements, or medications) that do not target a disease but may assert claims about cognitive enhancement or maintaining cognitive abilities such as memory or attention.**

Recommendation 6: ***Develop and Implement Core Competencies and Curricula in Cognitive Aging for Health Professionals***

The Department of Health and Human Services, the Department of Veterans Affairs, and educational, professional, and interdisciplinary associations and organizations involved in the health care of older adults (including, but not limited to, the Association of American Medical Colleges, the American Association of Colleges of Nursing, the National Association of Social Workers, the American Psychological Association, and the American Public Health Association) should develop and disseminate core competencies, curricula, and continuing education opportunities, including for primary care providers, that focus on cognitive aging as distinct from clinical cognitive syndromes and diseases, such as dementia.

Recommendation 7: ***Promote Cognitive Health in Wellness and Medical Visits***

Public health agencies (including the Centers for Disease Control and Prevention and state health departments), health care systems (including the Veterans Health Administration), the Centers for Medicare & Medicaid Services (CMS), health insurance companies, health care professional schools and organizations, health care professionals, and individuals and their families should promote cognitive health in regular medical and wellness visits among people of all ages. Attention should also be given to cognitive outcomes during hospital stays and post-surgery.

Specifically, health care professionals should use patient visits to:

- identify risk factors for cognitive decline and recommend measures to minimize risk; and review patient medications, paying attention to medications known to have an impact on cognition;
- provide patients and families with information on cognitive aging (as distinct from dementia) and actions that they can take to maintain cognitive health and prevent cognitive decline; and
- encourage individuals and family members to discuss their concerns and questions regarding cognitive health.

In addition, other components of the health care system have a cognitive health promotion role:

- CMS should develop and implement demonstration projects to identify best practices for clinicians in assessing cognitive change and functional impairment and in providing appropriate counseling and prevention messages during, for example, the Medicare Annual Wellness Visit or other health care visits.
- Health care systems and private and public health insurance companies should develop evidence-based programs and materials on cognitive health across the life span.
- During and after hospital stays and post-surgery, health care providers, patients, and families should be alert to potential cognitive changes and delirium.

Recommendation 8: ***Develop Consumer Product Evaluation Criteria and an Independent Information Gateway***

The Centers for Disease Control and Prevention, National Institutes of Health, and the Administration for Community Living, in conjunction with other health and consumer protection agencies, nonprofit organizations, and professional associations, should develop, test, and implement cognitive aging information resources and tools that can help individuals and families make more informed decisions regarding cognitive health.

Specifically,

- A central, user-friendly, easily navigated website should be available to provide independent, evidence-based information and links relevant to cognitive aging, including information on the promotion of protective behaviors and links to effective programs and services. The information should be presented in a way that takes health literacy into account.

- Consumer-relevant criteria should be developed and widely disseminated to provide individuals and families with guidance on evaluating cognition-related products (e.g., cognitive training products, nutriceuticals, and medications).

Recommendation 9: ***Expand Services to Better Meet the Needs of Older Adults and Their Families with Respect to Cognitive Health*** **Relevant federal and state agencies (including the Administration for Community Living [ACL], the Centers for Disease Control and Prevention [CDC], the National Highway Traffic Safety Administration [NHTSA], and the Consumer Financial Protection Bureau), nonprofit organizations (such as the Financial Industry Regulatory Authority), professional associations, and relevant private-sector companies and consumer organizations should develop, expand, implement, and evaluate programs and services used by older adults relevant to cognitive aging with the goal of helping older adults avoid exploitation, optimize their independence, improve their function in daily life, and aid their decision making.**

Specifically,

- Financial decision making:
    - The banking and financial services industries and state and federal banking and financial regulators should develop and disseminate banking and financial policies, services, and information materials that assist older adults and their families in making decisions that meet their financial means and objectives, that reduce the opportunities for unsuitable decisions, and that mitigate the harms of such decisions.
    - Surrogacy mechanisms, such as powers of attorney or multiparty accounts, should have appropriate safeguards to protect the interests of the older adult.
    - The financial services industries and relevant state and federal agencies should develop, strengthen, and implement systems approaches, best practices, training, and laws and regulations to help verify that financial transactions are not fraudulent or the result of diminished capacity or undue influence.
    - Systems should be strengthened for reporting or taking other protective actions against potential financial fraud, exploitation, or abuse to relevant enforcement and investigative officials. Laws and regulations should be revised to mitigate civil liability and professional harms resulting from such protective actions.
- Driving and transportation:
    - NHTSA, states' departments of motor vehicles, and relevant professional and consumer organizations such as the American Automobile Association should expand, validate, and disseminate tools and informational materials to assist older adults in maintaining and assessing their driving skills and to assist older adults and their families in making decisions about safe driving.
    - The automobile industry should expand and evaluate technologies that enhance decision making and safety for older drivers.
    - State and local transportation authorities, local planning commissions, private developers, and community groups should expand efforts to develop and implement alternative transportation options to accommodate changes that occur with cognitive aging, including efforts to ensure safe and walkable communities.
- Technology:
    - Technology industries should develop and adapt hardware, software, and emerging technologies to accommodate the needs of older adults that are related to cognitive aging.
    - The CDC, ACL, and other relevant agencies, organizations, and private-sector companies should support evidence-based programs that educate older adults in the use of emerging technologies.
- Health information:
    - Health information providers, including private-sector companies and government agencies, should ensure that their websites (including patient health portals), packaging (including medication packaging), and other consumer health information relevant to cognitive aging meet health literacy standards.

Recommendation 10: ***Expand Public Communication Efforts and Promote Key Messages and Actions***

The Centers for Disease Control and Prevention, the Administration for Community Living, the National Institutes of Health, other relevant federal agencies, state and local government agencies, relevant nonprofit and advocacy organizations and foundations, professional societies, and private-sector companies should develop, evaluate, and communicate key evidence-based messages about cognitive aging through social marketing and media campaigns; work to ensure accurate news and

storylines about cognitive aging through media relations; and promote effective services related to cognitive health in order to increase public understanding about cognitive aging and support actions that people can do to maintain their cognitive health.

Public communications efforts should:

- Reach the diverse U.S. population with campaigns and programs targeted to all relevant groups;
- Be sensitive to existing differences in knowledge, literacy, health literacy, perceived risk, cognitive aging–related behavior, communication practices, cultures and beliefs, speech and hearing declines, and skills and self-efficacy among target groups;
- Include evaluation components to assess outreach efficacy in the short and long term, and research the optimal communication strategies for the key messages among the target groups;
- Be updated as new evidence is gained on cognitive aging;
- Emphasize a lifelong approach to cognitive health;
- Promote succinct and actionable key messages that are understandable, memorable, and relevant to the target groups;
- Focus on sustaining changes in behaviors that promote cognitive health; and
- Promote effective evidence-based tools for maintenance of cognitive health and cognitive change assessment, as well as the information gateway on cognitive aging (see Recommendation 8).

McKnight Brain Research Foundation
Abbreviated History
March 2025

1. Established by Evelyn F. McKnight through a Trust Agreement dated May 26, 1999. Henry H. Raattama, Jr., Esquire, represented Mrs. McKnight.

2. Purpose: ***"…to provide support for medical research of the brain to accomplish alleviation of memory loss of the aging, including making grants to charitable organizations involved in such research."***

3. The trustee agreement specified three named "founding" trustees and one corporate trustee.
   Founding Trustees:
   A. J. Lee Dockery, M.D., retired obstetrician and gynecologist, medical administrator and educator.
   B. Nina Ellenbogen Raim, M.D., J.D., retired pediatrician, and attorney.
   C. Michael L. Dockery, M.D., practicing orthopedic surgeon.
   D. SunTrust Bank, Corporate Trustee.

4. June 25, 1999 -- Trust Document amended to specify a minimum of three trustees and a maximum of five trustees plus one corporate trustee.

5. April 28, 2000 -- First Gift Agreement for the MBRF with the University of Florida included a match by the State of Florida creating an endowment.

6. May 1, 2004 -- Second Gift Agreement for the MBRF with the University Alabama at Birmingham.

7. April 2005 -- "Qualifications for New Trustee" were adopted unanimously by the trustees. (The most current version of this document is included in the orientation packet.)

8. May 6, 2006—Approved a Research Partnership in Cognitive Aging between the McKnight Brain Research Foundation and the National Institute on Aging (NIA) through the Foundation for the National Institutes of Health (FNIH) to support a grant making program supporting research in age-related cognitive decline and memory loss. The Research Partnership in Cognitive Aging was approved for five years with a commitment of funding by the MBRF of $5 million payable $1 million annually and a minimum of $5 million from NIA, payable $1 million annually.

9. October 17, 2006 -- Third Gift Agreement for the MBRF with the University of Arizona.

10. December 24, 2006 – Fourth Gift Agreement for the MBRF with the University of Miami.

11. January 1, 2006 -- John G. Clarkson, M.D., was appointed as the fourth trustee. Dr. Clarkson was previously senior vice president for medical affairs and dean of the University of Miami Leonard M. Miller School of Medicine, and former director of UM's the Bascom Palmer Eye Institute and chairman of the Department of Ophthalmology. (Mr. and Mrs. McKnight had made a large gift to the Bascom Palmer Eye Institute to establish the William L McKnight Vision Research Center.)

12. April 1, 2009 -- Judith A. Salerno, M.D., M.S., was appointed as the fifth trustee. (Dr. Salerno was the former director of the National Institute on Aging and, in 2009, was the current Leonard D. Schaeffer Executive Officer of the Institute of Medicine of the National Academies.)

13. July 20, 2011 -- Dr. Clarkson's resignation was accepted by the trustees.

14. April 1, 2012 -- Dr. Salerno's second term was not renewed by the trustees.

15. April 11, 2012 -- Gene Ryerson, M.D., was appointed trustee replacing Dr. Clarkson. (Dr. Ryerson is a retired professor in pulmonary medicine from the University of Florida and the recipient of many outstanding teaching awards by the medical students.)

16. August 8, 2012 -- Robert M. Wah, M.D., was elected to replace Dr. Salerno as fifth trustee. Dr. Wah is a reproductive endocrinologist and obstetrician and gynecologist and, in 2012, was the Chief Medical Officer of North American Public Sector and Vice President of North American Public Sector at DXC Technology Company. Robert was President of the American Medical Association from June 2014-June 2015.

17. October 31, 2012—Approved the extension of the contract for the Research partnership in Cognitive aging for another five years under the same financial commitments of $5 million by the MBRF payable at $1million annually and a minimum of $5 million from the NIA also payable $1 million annually.

18. October 14, 2014 -- The trustees voted to abolish the consensus form of board governance and to establish a Board Chair, Vice Chair and Secretary position.

A. Dr. Lee Dockery was elected Board Chair.
B. Dr. Michael Dockery was elected Vice Chair.
C. Ms. Cianciotto, Corporate Trustee, to serve as the Secretary.

Terms of Office:

1. Two years of active service as a trustee member are required before becoming an officer.
2. An individual eligible to serve as an officer may be nominated by another trustee or self-nominate.
3. The term of office coincides with the fiscal year.
4. The term of the office of the chair is two years, but the number of terms not limited.

19. February 15, 2015--Trust Document amended to specify a minimum of three trustees and a maximum of seven trustees plus one corporate trustee.

20. April 29, 2015 -- Dr. Gene Ryerson was unanimously re-elected MBRF Trustee for a second three-year term.

21. August 12, 2015 -- Madhav Thambisetty, M.D., Ph.D., a neurologist and clinical pharmacologist was elected sixth trustee. Dr. Thambisetty is also director of Clinical and Translational Neuroscience within the Laboratory of Behavioral Neuroscience at the NIA and is an adjunct associate professor of neurology at the John's Hopkins University School of Medicine in Baltimore, Maryland.

22. August 12, 2015 -- Robert M. Wah, M.D., was unanimously re-elected MBRF Trustee for a second three-year term

23. April 27, 2016 -- Richard S. Isaacson, MD, a clinical neurologist and distinguished medical educator was elected seventh trustee. Dr. Isaacson currently serves as Director of the Neurology Residency Training Program and Director of the Alzheimer's Prevention Clinic, Weill Cornell Memory Disorders Program and Associate Professor of Neurology at Weill Cornell Medicine and New York-Presbyterian. Prior to his move to Cornell, Dr. Isaacson was Associate Professor of Clinical Neurology, Vice Chair of Education, and Education Director of the McKnight Brain Institute in the Department of Neurology at the University of Miami (UM) Leonard M. Miller School of Medicine.

24. April 5, 2017 -- The Trustees approved the funding of two Clinical Translational Scholars per year with the American Academy of Neurology (AAN) through the American Brain Research Foundation. Each scholarship is for a period of two years for a total of $150,000 with an additional $30,000 administrative cost payable to the American Brain Foundation. The name of the scholarship is the McKnight Clinical Translations Research Scholarship in Cognitive Aging and Age-related Memory Loss.

25. June 1, 2017 -- The contract was signed between the American Brain Foundation and the MBRF for the recruitment and management of the McKnight Clinical Translation Research Scholarship program.

26. February 21, 2018 -- Susan L. Pekarske, M.D., a clinical pathologist with a specialty in hematology was elected as trustee. The effective date of Dr. Pekarske's appointment was undetermined at the time subject to her personal commitments and the terms of service of the existing trustees within the MBRF.

27. April 1, 2018 -- Amy Porter was appointed executive director of the MBRF. Amy has served as a non-profit professional for over 30 years with 16 years' experience serving as executive director and CEO of two national, health-related organizations – the Foundation for the National Institutes of Health (FNIH) from 2001-2010 and the National Osteoporosis Foundation (NOF) from 2010 through 2017.

28. April 4, 2018 -- Dr. Gene Ryerson was unanimously re-elected MBRF Trustee for a third and final three-year term.

29. May 8, 2018 -- The Trust Document was amended to specify a minimum of seven trustees and a maximum of eleven trustees plus one corporate trustee.

30. July 1, 2018 -- Dr. Pekarske began her first three-year term of service as trustee of the MBRF.

31. July 16, 2018 -- Dr. Robert Wah was unanimously re-elected MBRF Trustee for a third and final three-year term.

32. July 16, 2018 -- Dr. Madhav Thambisetty was unanimously re-elected MBRF Trustee for a second three-year term.

33. October 23, 2018 -- Research Partnership in Cognitive Aging III contract was renewed with the National Institute on aging through the Foundation or the National Institutes of Health. The third research partnership project will jointly fund research to "Establish a Network for Identification, Evaluation and Tracking of Older Persons with Superior Competent Performance for their Chronological Age.

34. October 30, 2018 -- The Board of Trustees approved a reorganization plan to establish five standing committees of the Board to operationalize the activities and responsibilities of the Board. The following committees were established with each to be chaired by a trustee appointed by the Chair of the Board.

Chair of the Board. Each trustee is expected to serve on at least one standing committee. (This was changed to "expected to serve on at least two committees" on July 22, 2020.)

1. Membership and Governance
2. Finance
3. Education
4. Research
5. Communications

35. July 25, 2018 -- Dr. Lee Dockery was unanimously re-elected to a two-year term as Chair. Dr. Michael Dockery is unanimously re-elected to a two-year term as Vice Chair.

36. October 30, 2018 -- The Trustees approved a two-year communications plan with a budget not to exceed $300,000 which included the services of Valerie Patmintra, senior communication advisor.

37. April 10, 2019 -- Dr. Lee Dockery, founding trustee and Chair of the Board of Trustees of the MBRF, retired and was elected Chair Emeritus.

38. April 10, 2019 -- Dr. Michael L. Dockery, founding trustee and formerly Vice Chair of the MBRF was elected as the new Chair. Election to fill the vacant Vice Chair position was delayed until the July 2019 meeting of the trustees.

39. April 10, 2019 -- Nina Ellenbogen Raim, M.D., J.D., founding trustee of the MBRF resigned as trustee and was elected Trustee Emerita as an honorary status without specific duties and without compensation.

40. April 10, 2019 -- Dr. Richard Isaacson was unanimously re-elected MBRF Trustee for a second three-year term.

41. July 31, 2019 -- Dr. Madhav Thambisetty was unanimously elected as Vice Chair for a two-year term.

42. October 23, 2019 -- Funding was approved for the Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship at the University of Miami at $100,000 per year for a total of two years.

43. February 5, 2020 -- The trustees approved up to two mid-career research investigator awards. The *McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss will* focus on the "mature end of the spectrum" of clinical research and human studies. Funding will be available to researchers outside the MBIs as well as to those within the MBIs. Each year, one award will be made to support studies focusing on clinical translational research and another towards understanding basic biological mechanisms underlying cognitive aging and age-related memory loss. The awards will be up to $250,000 per year, per investigator, for three years from the MBRF to be matched by the host institution in equal amounts.

44. February 5, 2020 -- The trustees approved the recommendation for the education committee to be responsible for identifying and developing informational resources to be made available to primary care providers and the public.

45. February 5, 2020 -- The trustees approved the additional budget request from the University of Arizona to support additional requirements for resubmission of the Precision Aging Network Pilot Proposal not to exceed $250,000.

46. October 1. 2020 – Dr. Patricia Boyle was unanimously elected to her first term as Trustee.

47. October 14, 2020 -- The trustees approved renewal of the partnership with the American Brain Foundation for 5-years with a $1,650,000 grant to support 10 additional McKnight Clinical Translational Research Scholarships from 2023 – 2028.

48. November 1, 2020 – Dr. Allison Brashear was unanimously elected to her first term as Trustee.

49. February 26, 2021 -- The trustees approved the renewal contract with the American Brain Foundation for the administration and management of the of McKnight Cognitive Aging and Memory Clinical Translation Research Scholarship in Cognitive Aging and Age-Related memory Loss through the American Academy of Neurology.

50. February 26, 2021 -- The trustees approved the American Federation for Aging Research (AFAR) for the management and administration for the Mid-Career Investigator Awards.

51. April 9, 2021 -- The contract was signed with American Federation for Aging Research

52. April 30, 2021 -- Added the word "Innovator" to the Mid-Career Awards – the name is the ***McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss.***

53. April 30, 2021 -- Gene Ryerson, MD, completed his third and final term as trustee of the MBRF. Dr. Ryerson received a proclamation and an inscribed Tiffany Crystal Bowl in recognition of nine years of dedicated service to the MBRF.

54. July 28, 2021 -- Robert M. Wah, MD, completed his third and final term as trustee of the MBRF. Dr. Wah received a Proclamation and an inscribed display cabinet for medals in recognition of nine years of dedicated service to the MBRF.

55. October 23, 2019 -- The trustees approved a proposal for a one-time funding in the amount of $200,000 to launch the *Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship*. The grant is for $100,000 annually for a period of two years for a total not to exceed $200,000.

56. October 28, 2021 -- The trustees approved a one-time funding to establish the *Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging* postdoctoral training program in the amount of $250,000 to be matched by the University of Miami. The grant is for $50,000 annually for a period of five years for a total not to exceed $250,000 with the understanding recruitment for the scholars will be from a national qualified applicant pool and efforts would be made to retain the successful scholars as clinical science faculty.

57. December 7, 2021 –John E. Brady, MD, was unanimously elected to the Board of Trustees for a three-year appointment to begin January 1, 2022.

58. February 1, 2022--Amy Porter, executive director of the MBRF, since April 1, 2018, announced her intended retirement by December 31, 2022, but not later than the end of her contract year, April 1, 2023.

59. March 23, 2022—The Membership and Governance Committee requested approval by the Trustees of the concept of hiring an Educational Advisor to advance the educational outreach initiative to Primary Care Provider (PCP) similar to the function of the MBRF Senior Communications Advisor. After discussion, the Trustees approved the development of and RFA for an education advisor consultant to assist the MBRF in understanding the educational environment in defining the scope of what the MBRF can or hope to accomplish with an Education Initiative and the required credentials for an Education Advisor.

60. August 15, 2022 -- Angelika Schlanger, PhD, was appointed as executive director of the MBRF. Dr. Schlanger served with distinction as the inaugural director of the Frederick A. DeLuca Foundation for four years prior to joining the MBRF.

61. October 1, 2022 -- Amy Porter officially retired from her position as the first executive director of the MBRF.

62. September 20, 2022—After review of several requested proposal from different organizations, the Trustees approved the engagement of the Strategic Communications and Planning, Inc. (SCP) agency to expand the educational outreach on age related cognitive decline and memory loss to Primary Care Providers and the consumer with a budget not to exceed $40,000.

Specifically, the SCP proposal was designed to**:**

- Conduct a landscape analysis of the educational resources and assessment tools available to primary care providers (PCPs) related to cognitive aging and brain health; and
- Make a series of specific, short-, mid- and long-term recommendations that MBRF can pursue to encourage PCPs to make brain health assessments and education a more regular part of their practices and educate the consumer about the importance of brain health integrated within personal health maintenance behavior.

63. February 16, 2023-- Strategic Communications and Planning, Inc (SCP) presented report to Board of Trustees. The Trustees authorized the Executive Director to proceed with outreach to organizations aligned with existing education efforts directed to consumers/patients, and those directed to Primary Care Provides (PCPs).

64. February 16, 2023--The trustees authorized the Executive Director to pursue the recommended strategies #1 (Consumer Health/Consumer Education Initiative) and #2 (Primary Care Education and Practice Models/Approaches) from the SCP Scoping Document and to incorporate strategy #3 (PCP Public Information Campaign) within a three-year communications plan.

65. March 31, 2023 -- Richard S. Isaacson, MD, after seven years of dedicated service resigned his position as trustee of the MBRF.

66. April 17, 2023—Sharon Brangman, MD and Roy H. Hamilton, MD, MS are unanimously elected to the Board of Trustees for three-year appointment to begin July 1, 2023

67. May 3, 2023—After intensive review of five proposals for a Public Information Campaign for Primary Care Providers, the BRG Communications Agency was selected to manage the project to enhance and expand a three-year communications plan at a budget level of $1.75 million over the three years, including consulting fees.

69. May 3, 2023--The Trustees reviewed proposals from aligned organizations with existing educational programs and curricula interested in partnering with the MBRF by using the MBRF Key Messages in developing a stand-along brain health module or incorporate the module into existing curricula designed for consumers and patients.

70. May 3, 2023—After discussion, the Trustees recommended the Self-Management Resource Center (SMRC) be invited to submit a concept paper or proposal and budget for the partnering with the MBRF in the development of educational materials in brain health directed toward patients and consumers.

The Self-Management Resource Center is the culmination of 40 years of research and program development, all focused on the goal of helping people better manage their chronic health conditions.

71. May 3, 2023---The Proclamation to Richard S. Isaacson, MD recognizing his seven years of service to the MBRF approved at the March 31, 2023 meeting, was presented and read into the minutes of May 3, 2023 Trustees' meeting.

72. May 3, 2023—The Trustees unanimously approved the re-election of Michael Dockery, MD as Chair and Madhav Thambisetty, MD, PhD as Vice Chair for three year terms from July 1, 2023 to June 30. 2025.

73. July 24, 2023—The Trustees approved the retention of Robert H. Wall, Esquire, as legal counsel for the MBRF. Mr. Wall is a law partner with the Akerman Law firm located in Winston Salem, NC. Link to Mr. Wall's Bio: https://www.akerman.com/en/people/robert-wall.html

74. July 24, 2023—Trustees approved a request for proposals from a facilitator to lead a strategic planning process for the MBRF with budget to be reviewed and approved by the finance committee.

75. October 22, 2023---Patricia Boyle, PhD and Allison Brashear, MD, MBA re-appointments as trustees were unanimously approved for another three years beginning October 1, 2023 and concluding September 30, 2026.

76. September 30, 2023—Following the death in January 2023 of Dr. Ralph Sacco, Executive Director of the Evelyn F. McKnight Brain Institute (EMBI) at the UM, Dr. Tatjana Rundek was appointed interim Director until at which time the Chair of the Department of Neurology could be filled. in a written communication from Dr. Rundek, announced the reorganization of the leadership of the EMBI at UM as follows: Tatjana Rundek, MD, PhD, Director, and Dr. Bonnie Levin, PhD and Dr. Ihtsham Ul Haq, MD as Co-Associate Directors of the University of Miami EMBI. Both Dr. Rundek and Dr. Levin have been strong advocates for the MBRF and Dr. Haq has received support from the MBRF for his fellowship in Brain Health and Aging

77. October 23, 2023—The Trustees approved the strategic plan developed with facilitator Stephen Ferrante, Victory Group LLC. Link to website: https://www.groupvictory.net/bios/stephen-ferrante

As an outcome to the strategic planning process the current role and qualifications of the executive leadership was questioned as to the ability to advance the MBRF's Mission…"*To enhance life by preserving memory and supporting healthy cognitive aging through research and education*".

78. February 1-4, 2024—25th anniversary celebration of the founding of the Brain Institute at the University of Florida in 1999 and named for William L. and Evelyn F. McKnight in 2000. The MBRF in conjunction with the UF celebrated its 25th anniversary. The following are links to short videos recognizing the 25th Anniversary for both the UF and the MBRF

MBRF 25th Anniversary Video UF MBI 25th Anniversary Video

79. February 20, 2024—Trustees approved the proposal from the Cognitive Aging and Memory Interventional Core committee to increase the Pilot Grant Awards from $60,000 per year to $75,000 per year for the two-year grant period.

80. February 20, 2024---Trustees approved a budget of $4,400 to host a dinner in conjunction with the Annual Meeting of the American Academy of Neurology for the McKnight Clinical Translational Research Scholars funded by the MBRF awarded through the American Brain Foundation.

81. March 19, 2024---The trustees approved an amount not to exceed $15,000 for the MBRF 25th Anniversary Celebration. The funds are to cover the costs of an Anniversary video by BRG and several items at the Inter-Institutional Meeting and Cognitive Summit IV.

82. March 19, 2024--- The proposal is to renew the current Innovator Awards grant for another three years in the amount of $4,626,500 for three additional cohorts of investigators (6 total). The proposed budget represents an increase of $11,500 in administrative costs

83. March 20-21, 2024--- The Cognitive Aging Summit IV was held in Bethesda, MD. This fourth Summit was devoted to scientific presentations and discussion of age-related brain and cognitive change, with a particular focus on individual differences and the development of personalized approaches to the remediation of decline and the maintenance of brain health.

The program content and video-recordings of the Summit can be viewed on the link below.

https://www.nia.nih.gov/research/dn/cognitive-aging-summit-iv

84. March 22, 2024—MBRF launched a new National Campaign – **Brain Works: Optimize Your Brain Span –**developed in to "*Educate the Public on Cognitive Aging and How to Keep the Brain Healthy."*

85. May 15, 2024—The trustees unanimously approved the three-year appointment of Madhav Thambisetty, MD, PhD as Trustee effective August 12, 2024, concluding August 11, 2027.

86. May 15-17, 2024--16th Inter-Institutional meeting was held at the William L. and the Evelyn F. McKnight Brain Institute of the University of Florida. See Links to program and press release below:

Draft 2024 Inter Institutional Meeting Agenda.pdf

https://mbi.ufl.edu/2024/05/20/mcknight-brain-research-foundation-meeting-convenes-top-cognitive-aging-researchers/

87. July 18, 2024-- The Trustees, after discussions over several months following the approval of the Strategic plan on October 23, 2023, concluded the duties of Chief Operating Officer were more aligned than the Executive Director position to advance the mission and purpose of the MBRF.

88. July 18, 2024---A search committee was formed and held its first meeting charged with developing a position description of a CEO and to proceed with the process of recruitment of a qualified person to fill the position. Search Committee members: J. Lee Dockery, MD, Chair and Members: Michael Dockery, MD (Chair of the Board of Trustees), John Brady, MD; Sharon Brangman, MD; Allison Brashear, MD, MBA; Melanie Cianciotto (Corporate Trustee) and Amy Porter, (Interim Executive Director).

89. August 15, 2024— The position of Executive Director (ED) was abolished, and the position of Chief Executive Officer (CEO) was established. The contract for the current ED expired on August 15, 2024, and it was not renewed.

90. August 15, 2024—Amy Porter, the former Executive Director who had retired October 1, 2022, agreed to return as a part-time Interim Executive Director until the position description and the successful search process was concluded for the recruitment of a qualified person to fill the CEO position.

91. July 25, 2024---The Trustees approved the recommendation of the Search Committee to select the Executive Search Team from the Spencer Stuart firm for an approved budget for the project not to exceed $165,000. The budget breakdown is as follows: $130,000 minimum professional fee, 10% administrative fee, plus direct expenses

92. September 12, 2024—The position description for the CEO position for the MBRF was approved. Link to copy of position description: MBRF CEO 66286-001 SPC_Final.pdf

93. November 4, 2024—Search Committee members reviewed pool of candidates with Spencer Stuart Team and seven candidates were selected for virtual interview.

94. November 6, 2024-December 18, 2024—Seven worthy candidates for the CEO position were interviewed virtually and three were selected for in-person interviews.

95. January 18, 2025- Following background checks and initial references by the Spencer Stuart Team, the three candidates, with all search committee members present, were interviewed. Each candidate made a presentation regarding their respective qualifications and vision for the future of the MBRF under their leadership.

96. February 19, 2025—Alice Luo Clayton, PhD, a distinguished neuroscientist, was selected and accepted the “letter of offer” to become the inaugural CEO of the MBRF. Link to CV and Statement of interest in the CEO position Alice-Luo-Clayton.pdf

97. March 14, 2025—The contract was signed by Alice Luo Clayton, PhD to become the inaugural CEO of the MBRF with a starting date of April 28, 2025

Duties and Responsibilities
of
Individual Trustees

McKnight Brain Research Foundation (MBRF)
Board of Trustees
Individual Trustee Duties and Responsibilities

Duties: To advise, govern, oversee policy and direction, and assist with the leadership and promotion of the McKnight Brain Research Foundation (MBRF) in support of the organization's vision, mission and goals. As a board member, passion, participation and commitment are vital to the success of the Foundation. A board member's effectiveness will be enhanced by striving to be knowledgeable about the trends and research initiatives in cognitive aging and associated memory loss in the aging.

Responsibilities: Leadership, Governance and Oversight:

1. Understand and support the Vision, Values, and Mission of the MBRF.
2. Adhere to the Code of Ethics, avoid or report Conflicts of Interest.
3. Understand and review periodically the Policies and Procedures of the MBRF.
4. Review agenda, financial information, and supporting material in advance of the trustee meetings or committee meetings.
5. Ensure fiscal oversight and integrity with review and approval of the MBRF annual operating budget, major expenditures, investment of funds, and any related financial responsibilities.
6. Provide oversight of the MBRF; monitor and evaluate the effectiveness of funded institutes and programs through a regular review, completed at least on a yearly basis.
7. Serve as an advocate for the MBRF and foster collegial relationships with its institutes and partners, the scientific community, and state and federal officials.
8. Attend and participate in all MBRF trustee meetings – usually four a year – focusing attention on the discussion and matters at hand.
9. Attend and participate as a member of at least two committees of the Board of Trustees.
10. Ensure that each topic on the meeting agenda receives sufficient attention and that communication is collegial and contributes to the effectiveness and cohesiveness of the group.
11. Respond in a timely manner (within 2 business days) to emails from other Trustees or staff regarding ongoing assignments, work of the committees, reviews, reports or voting by email.
12. Identify and share names of individuals with relevant skills and experience to be considered as potential nominees for Trustee positions; and share names of organizations and foundations which may be potential program or funding partners with the MBRF.
13. At the direction of the MBRF Chair, act as representative or spokesperson for the MBRF to partners or other constituencies; take advantage of opportunities to enhance the organization's public image through interviews, content for the MBRF website, presentations, and highlighting your role as a Trustee.
14. Monitor and provide feedback, insights, or direction as requested or needed. Maintain a good working relationship with other Trustees, the Corporate Trustee, the Executive Director and staff and advisors.
15. Participate in setting annual goals for the MBRF, in strategic planning, vision setting, and evaluation efforts.

Length of Term: Three (3) years, which may be renewed for additional terms, pending approval of the Board of Trustees, for a maximum of nine (9) years.

Approved April 6, 2015
Length of Term Approved July 31, 2019, Trustees Meeting
Responsibilities Amended and Approved July 22, 2020, Trustees Meeting

McKnight Brain Research Foundation (MBRF)
Code of Ethics

The McKnight Brain Research Foundation is committed to:

- Act honestly, truthfully and with integrity in all transactions and dealings.
- Promote the avoidance of conflicts of interest and commit to the appropriate handling of actual or apparent conflicts of interest in all relationships.
- Treat all grantees fairly and treat every individual with dignity and respect.
- Be a good corporate citizen and to comply with both the spirit and the letter of the law.
- Act responsibly toward the professional communities in which we work and for the benefit of the professional communities we serve.
- Be responsible, transparent, and accountable for all of our actions.
- Attend all regularly scheduled board meetings insofar as possible, and become informed concerning the issues to be considered at those meetings.
- Endeavor to make policy decisions only after full discussion.
- Render all decisions based on the available facts and independent judgment, and refuse to surrender that judgment.
- Encourage the free expression of opinion by all board members, and seek systematic communications among the board members.
- Work with other board members to establish effective board policies and to delegate authority as appropriate.
- Stay informed about pertinent issues by individual study and through participation in programs providing needed information relevant to the MBRF.
- Take no private action that will compromise the Foundation, and respect the confidentiality of information that is privileged under applicable law.
- Monitor and evaluate on a regular basis the MBRF actions and activities.
- Ensure that the resources of the Foundation are responsibly and prudently managed.
- Adopt and monitor spending practices and investment policies which are fair, reasonable and appropriate to fulfill the mission of the Foundation.

Adopted May 18, 2005
Reaffirmed July 22, 2020

McKnight Brain Research Foundation
Conflict of Interest Policy

ARTICLE I
Purpose

The purpose of this Conflict of Interest Policy is to protect the interest of the McKnight Brain Research Foundation ("MBRF") when it is contemplating entering into a transaction that may benefit the private interest of a MBRF Trustee. This Conflict of Interest Policy is intended to supplement, but not replace, any applicable state and federal laws governing conflicts of interest applicable to MBRF including, specifically, Section 617.0832, Fla. Stat. and Section 4941 of the Internal Revenue Code of 1986, as amended.

ARTICLE II
Conflict of Interest

A Trustee has a conflict of interest with respect to a proposed transaction if completion of the transaction would directly or indirectly benefit the Trustee or an affiliate of the Trustee. Benefit for this purpose means a financial benefit. Affiliate for this purpose means all members of the Trustee's immediate family or a business entity 35% or more of which is owned by the Trustee.

ARTICLE III
Disclosure

If a Trustee has an interest in a possible transaction, such interest shall be disclosed to all Trustees ("Disclosing Trustee"). The Trustees, other than the Disclosing Trustee, shall decide whether the transaction giving rise to the potential conflict is, on balance, in the best interest of MBRF. The Trustees shall be free to consult with the Disclosing Trustee to fully understand the proposed transaction and the circumstances giving rise to the conflict.

After full disclosure and appropriate due diligence, the Trustees, other than the Disclosing Trustee, shall vote on the transaction using the same criteria for approval or disapproval as is used for any transaction. If the Trustees believe the transaction to be in the best interest of MBRF, the Trustees shall be free to approve the proposed transaction notwithstanding the conflict.

ARTICLE IV
Customary Business Practices

In no event shall receipt of a benefit that is a customary business practice be considered a conflict. A customary business practice means a business related gift, such as a meal, of a type customarily provided in the context within which the business related gift is provided.

ARTICLE V
Compensation

It is recognized the setting of Trustee compensation by Trustees is an inherent conflict. Because of the MBRF organizational structure, it is not possible to cause compensation to be decided by independent trustees. In recognition of this inherent conflict, the Trustees shall annually review Trustee compensation and the basis used to establish Trustee compensation. The Trustees will research available comparables, if any, and such other third party information as is reasonably available. The Trustees shall record the basis for compensation and the amount of compensation.

ARTICLE VI
Annual Filing

Each member of the Board of Trustees shall file a statement annually setting forth any conflict of interest which might occur during the ensuing year. The statement shall disclose as fully as possible the nature of the potential conflict and the nature of the Trustees' interest in the possible transaction. The statements shall be circulated to all Trustees.

McKNIGHT BRAIN RESEARCH FOUNDATION
TRUSTEES' CONFLICT OF INTEREST STATEMENT

I have read the McKnight Brain Research Foundation Conflict of Interest Policy adopted by the Board of Trustees on the eighteenth of May, 2005. I agree to answer any questions the Board of Trustees may have with respect to any actual or potential conflict of interest and to otherwise abide by the Conflict of Interest Policy.

Check one of the following:

____ To the best of my knowledge, there exists no circumstances involving me or an affiliate that may be considered an interest in a transaction or possible transaction to be entered into by the McKnight Brain Research Foundation.

or

____ There does exist the following conflict of interest in a possible transaction:

_____

_____
Signature

_____
Date

McKnight Brain Research Foundation (MBRF)

Annual Trustee Responsibilities and Commitment Form

Trustee Name_____Year_____

Vision:

To: "Improve the quality of life through the understanding and alleviation of age-related memory loss."

Value Statement:

- ***Commitment***

The MBRF is committed to its vision to understand and alleviate age-related memory loss, and expects the same of its grant recipients and research partners.

- ***Discovery***

The MBRF values scientific curiosity and discovery leading to clinical intervention in age-related memory loss.

- ***Honesty/Integrity***

The MBRF conducts its affairs with the highest degree of honesty, integrity, and accountability and expects the same of others.

Mission:

Lead in generating interest and support of scientific research to understand and alleviate age-related memory loss.
Inspire commitment and shared vision in the understanding and alleviation of age-related memory loss.
Nurture scientists dedicated to the exploration of innovative research initiatives intended for clinical application in age-related memory loss.
Promote collaboration and communication among research scientists, institutions, and organizations engaged in research in age-related memory loss.
Partner with research scientists, institutions, and organizations to promote research to understand and alleviate age-related memory loss.
Recognize and Reward significant achievement in discoveries leading to clinical intervention to understand and alleviate age-related memory loss.

Code of Ethics

The McKnight Brain Research Foundation is committed to:

- Act honestly, truthfully and with integrity in all transactions and dealings.
- Promote the avoidance of conflicts of interest and commit to the appropriate handling of actual or apparent conflicts of interest in all relationships.
- Treat all grantees fairly and treat every individual with dignity and respect.
- Be a good corporate citizen and to comply with both the spirit and the letter of the law.
- Act responsibly toward the professional communities in which we work and for the benefit of the professional communities we serve.
- Be responsible, transparent, and accountable for all of our actions.
- Attend all regularly scheduled board meetings insofar as possible, and become informed concerning the issues to be considered at those meetings.
- Endeavor to make policy decisions only after full discussion.
- Render all decisions based on the available facts and independent judgment, and refuse to surrender that judgment.
- Encourage the free expression of opinion by all board members, and seek systematic communications among the board members.
- Work with other board members to establish effective board policies and to delegate authority as appropriate.
- Stay informed about pertinent issues by individual study and through participation in programs providing needed information relevant to the MBRF.

Code of Ethics, Continued

- Take no private action that will compromise the Foundation, and respect the confidentiality of information that is privileged under applicable law.
- Monitor and evaluate on a regular basis the MBRF actions and activities.
- Ensure that the resources of the Foundation are responsibly and prudently managed.
- Adopt and monitor spending practices and investment policies which are fair, reasonable and appropriate to fulfill the mission of the Foundation.

I understand my duties and responsibilities as a Trustee are to:

1. Understand and support the Vision, Values, and Mission of the MBRF.
2. Adhere to the Code of Ethics, avoid or report Conflicts of Interest.
3. Understand and review periodically the Policies and Procedures of the MBRF.
4. Review agenda, financial information, and supporting material in advance of the trustee meetings or committee meetings.
5. Ensure fiscal oversight and integrity with review and approval of the MBRF annual operating budget, major expenditures, investment of funds, and any related financial responsibilities.
6. Provide oversight of the MBRF; monitor and evaluate the effectiveness of funded institutes and programs through a regular review, completed at least on a yearly basis.
7. Serve as an advocate for the MBRF and foster collegial relationships with its institutes and partners, the scientific community, and state and federal officials.
8. Attend and participate in all MBRF trustee meetings – usually four a year -- focusing attention on the discussion and the matters at hand.
9. Attend and participate as a member of at least two committees of the Board of Trustees.
10. Ensure that each topic on the meeting agenda receives sufficient attention and that communication is collegial and contributes to the effectiveness and cohesiveness of the group.
11. Respond in a timely manner (within 2 business days) to emails from other Trustees or staff regarding ongoing assignments, work of the committees, reviews, reports or voting by email.
12. Identify and share names of individuals with relevant skills and experience to be considered as potential nominees for Trustee positions; and share names of organizations and foundations which may be potential program or funding partners with the MBRF.
13. At the direction of the MBRF Chair, act as representative or spokesperson for the MBRF to partners or other constituencies; take advantage of opportunities to enhance the organization's public image through interviews, content for the MBRF website, presentations, and highlighting your role as a Trustee.
14. Monitor and provide feedback, insights, or direction as requested or needed. Maintain a good working relationship with other Trustees, the Corporate Trustee, the Executive Director and all other staff and advisors.
15. Participate in setting annual goals for the MBRF, in strategic planning, vision setting and evaluation efforts.

I accept the above commitment as an understanding of my role and responsibilities as a member of the Board of Trustees.

Signature_____Date_____

McKnight Brain Research Foundation (MBRF)

Annual Trustee Self-Assessment

Vision:

To: "Improve the quality of life through the understanding and alleviation of age-related memory loss."

Trustee Name_____Year_____

Previously, I committed to executing my responsibilities as a Trustee of the MBRF to the following areas. Now, I'm using a scale of 1 to 3 with 3 representing excellence and leadership; 2 as needing more of my attention and/or greater involvement; and 1 as having not met the responsibilities and requirements of the role of Trustee.

I understand that my evaluation will be shared with the MBRF Chair and the Chair of the Membership and Governance Committee. I welcome their suggestions for how best to expand my understanding of and participation in the work of the MBRF and to uphold its Vision, Values, Mission and Code of Ethics.

As a Trustee, I:	Score 1 – 3
1. Understand and support the Vision, Values, and Mission of the MBRF.	
2. Adhere to the Code of Ethics, avoid or report Conflicts of Interest.	
3. Understand and review periodically the Policies and Procedures of the MBRF.	
4. Review agenda, financial information, and supporting material in advance of the trustee meetings or committee meetings.	
5. Ensure fiscal oversight and integrity with review and approval of the MBRF annual operating budget, major expenditures, investment of funds, and any related financial responsibilities.	
6. Provide oversight of the MBRF; monitor and evaluate the effectiveness of funded institutes and programs through a regular review, completed at least on a yearly basis.	
7. Serve as an advocate for the MBRF and foster collegial relationships with its institutes and partners, the scientific community, and state and federal officials.	
8. Attend and participate in all MBRF trustee meetings – usually four a year -- focusing attention on the discussion and the matters at hand.	
9. Attend and participate as a member of at least two committees of the Board of Trustees.	
10. Ensure that each topic on the meeting agenda receives sufficient attention and that communication is collegial and contributes to the effectiveness and cohesiveness of the group.	

11. Respond in a timely manner (within 2 business days) to emails from other Trustees or staff regarding ongoing assignments, work of the committees, reviews, reports or voting by email.	
12. Identify and share names of individuals with relevant skills and experience to be considered as potential nominees for Trustee positions; and share names of organizations and foundations which may be potential program or funding partners with the MBRF.	
13. At the direction of the MBRF Chair, act as representative or spokesperson for the MBRF to partners or other constituencies; take advantage of opportunities to enhance the organization's public image through interviews, content for the MBRF website, presentations, and highlighting your role as a Trustee.	
14. Monitor and provide feedback, insights, or direction as requested or needed. Maintain a good working relationship with other Trustees, the Corporate Trustee, the Executive Director and all other staff and advisors.	
15. Participate in setting annual goals for the MBRF, in strategic planning, vision setting and evaluation efforts.	

I acknowledge that in the areas in which I ranked less than a 3, it will be desirable for me to improve my performance through greater attention, involvement, and understanding. I commit to taking the following steps to improve in these areas. As needed, I will identify the areas in which I would benefit from additional information or mentoring to improve my performance. I look forward to a review of my participation and performance with the MBRF Chair.

_____

_____

_____

_____

_____

_____

I have the following suggestions for how the Board of Trustees might improve:

_____

_____

_____

_____

_____

_____ _____

Signature Date

McKnight Brain Research Foundation
Expense Reimbursement Policy

Trustee Reimbursement

The Trustees of the McKnight Brain Research Foundation (MBRF) will be reimbursed for any out of pocket expenses and travel costs associated with MBRF business.

1. Trustees will submit a MBRF Expense Report form when requesting reimbursement.
2. Trustees are responsible for providing receipts when requesting reimbursement for out of pocket documented expenses and travel costs associated with MBRF business.
3. Reimbursement should be requested within 60 days of the expense occurrence.
4. The MBRF Expense Report form and receipts should be sent to the Corporate Trustee for processing.

Executive Director Reimbursement

The Executive Director of the McKnight Brain Research Foundation (MBRF) will be reimbursed for any out of pocket expenses and travel costs associated with MBRF business.

1. The Executive Director will submit a MBRF Expense Report form when requesting reimbursement.
2. The Executive Director is responsible for providing receipts when requesting reimbursement for out of pocket documented expense and travel costs associated with MBRF business.
3. Reimbursement should be requested within 60 days of the expense occurrence.
4. The MBRF Expense Report form and receipts should be sent to the Corporate Trustee for processing.

Inter-Institutional Meeting Attendee Reimbursement

Attendees and invited guests will be reimbursed for any out of pocket documented expenses and travel costs associated with attending the Inter-Institutional Meeting. Reimbursement will not be provided for the following:

Rental Cars
Meals when a meal was provided as part of the meeting

1. Attendees will submit a Travel Expense Reimbursement form when requesting reimbursement.
2. Attendees are responsible for providing receipts when requesting reimbursement for out of pocket documented expenses and travel costs associated with attending the Inter-Institutional Meeting.
3. Reimbursement should be requested within 14 days following the conclusion of the Inter-Institutional Meeting.
4. The Travel Expense Reimbursement form and receipts should be sent to the Corporate Trustee for processing.

Failure to comply with this policy will result in no reimbursement of expenses.

Policy adopted July 31, 2019

Duties and Responsibilities of Officers, Executive Director, and Chief Executive Officer

Chair of the Board of Trustees

McKnight Brain Research Foundation

The role of the Chair of the Board of Trustees of the McKnight Brain Research Foundation (MBRF) is to manage and to provide leadership to the Board of Trustees (Board). The Chair is accountable to the Board and acts as a direct liaison between the Board and the Executive Director (ED) to ensure that the Board's directives and resolutions are executed. The Chair acts as the chief communicator for the Board's decisions to the ED.

The duties and responsibilities of the Chair in relation to the Board are to:

Lead the Board to carry out its governance functions, ensuring the duties of care, obedience, loyalty and are fulfilled;

Ensure the Board approves and updates policies, including the MBRF Corporate Trust Agreement, for sound and compliant governance of the organization;

Ensure the ongoing recruitment, development, contributions and evaluations of Board members;

Manage the assessment of the performance of the Board and its committees, conduct evaluations of the Board, and make recommendations to the Board annually, regarding the effectiveness of the Board as a whole, as well as the Committees of the Board and individual Trustees;

Coordinate the strategic planning process through oversight of, direction to and partnership with the executive director;

Preside over regular and special meetings of the Board;

Review and sign minutes of all Board meetings;

Appoint, with Board approval, all committees, task forces and other special project roles of Board members in support of the organization's strategic plan;

Serve as ex-officio member of all committees of the Board;

Serve as an ambassador of the organization and advocate its mission to internal and external stakeholders;

Lead Board member development and succession planning.

Approved 11/8/2017

The duties and responsibilities of the Chair in relation to the ED are to:

Act as a liaison between management and the Board;

Serve as a trusted advisor to and provide independent counsel to the ED;

Partner with the ED to ensure the Board's directives, policies, and resolutions are carried out in a timely manner;

Ensure that the ED keeps the Board informed and that sufficient information is provided to enable the Board to develop appropriate decisions;

Establish priorities, and jointly create with the ED, the agendas for meetings of the Board;

Jointly with ED, serve as a spokesperson, when appropriate;

Jointly with ED, foster relationships with organizations and grant recipients;

Coordinate an annual performance review of the ED.

Qualifications of the Chair of the Board

Vision and capacity to inspire other volunteers;

Objectivity to hear all sides, listen well and manage a forum for input;

Extensive knowledge of the organization and its mission and impact;

Passion for the mission of the organization;

Ability to co-lead with a ED the strategic planning of the organization;

Ability to lead meetings through consent agendas, issues management and committee management;

Excellent communication skills with the ED, fellow Board members, grantees and other stakeholder audiences;

Ability to understand and manage with good humor, in partnership with the ED, the boundaries between the ED and Board Chair roles and responsibilities.

Duties of Vice Chair
Board of Trustees
McKnight Brain Research Foundation (MBRF)

1. **Substitute for Chair**

2. **Other tasks as assigned by the Chair or designated by the Board**

Approved: April 6, 2015

Chair Emeritus
McKnight Brain Research Foundation
Position Description

For J. Lee Dockery, MD
Founding Trustee and
First Chair Emeritus of the McKnight Brain Research Foundation

June 2019

Chair Emeritus is a title conveyed by the Board of Trustees of the McKnight Brain Research Foundation (MBRF) upon a former Chair of the Board of Trustees. The title is meant to achieve two goals: to recognize the individual's visionary leadership and extraordinary service while serving as Chair, and to convey upon this individual a new role with the MBRF. The Chair Emeritus title recognizes past exceptional achievement in advancing the mission of the MBRF while signaling the continued activities of the title holder in a more focused, yet equally important, role as it relates to the foundation's future success.

In April 2019, on the 20th Anniversary of his appointment as a founding Trustee, Dr. J. Lee Dockery was named the first Chair Emeritus of the McKnight Brain Research Foundation. Dr. Dockery is a valuable source of wisdom and institutional memory as well as continuing to hold forth a clear vision for the future of the MBRF and the field of research in cognitive aging, age-related cognitive decline and memory loss.

The Trustees of the MBRF feel strongly that Dr. Dockery's voice, ideas, and reputational standing are essential to continuing to address the vision and mission of the MBRF and the McKnight Brain Institutes (MBIs). Therefore, the Trustees extend an open invitation to Dr. Dockery to attend meetings of the Board of Trustees and to participate in any events of the MBRF and the McKnight Brain Institutes which he finds of interest.

The Trustees request that Dr. Dockery, within his availability and interest, assume the role and duties of ambassador, spokesman, and representative for the MBRF and that he will continue to foster current relationships and cultivate new relationships with partners and partner organizations on the foundation's behalf. Specifically, the Trustees request that Dr. Dockery attend the annual Inter-institutional Meeting of the McKnight Brain Institutes (if the meeting site is accessible to him); that he will continue to communicate with the Institute of Medicine (IOM) Working Group relative to the Report on Cognitive Aging; and that he attend or participate in other events, conferences, and meetings that his schedule, interest, and travel restrictions permit.

It is requested that Dr. Dockery participate as a member of the Membership and Governance Committee to help identify and recruit new Trustees and to offer insight into the committee's work related to governance. It is desired by the Trustees for Dr. Dockery to lead the Trustees' approved orientation program for all new trustees. It is also requested that Dr. Dockery lend his voice to the efforts of the Education Committee to seek inclusion of core competencies in cognitive aging in curricula and licensing requirements for Health Professionals. As spokesperson, Dr. Dockery may be called upon to work with the Communications Working Group to develop or review historical content, as well as to characterize and communicate the vision behind current activities and programs.

As Chair Emeritus, Dr. Dockery's performance of the duties outlined for the position is intended to be as selective and or comprehensive as compatible with his interest and availability. Dr. Dockery will be compensated at the same rate as the Trustees for his performance and participation in the activities described above, including reimbursement of Travel and related expenses benefitting the MBRF. The Chair Emeritus serves at the pleasure of the Board. The term is self-renewing and does not require renewal by the Board of Trustees.

Duties of the Corporate Trustee/Secretary for the McKnight Brain Research Foundation (MBRF)

1. Appointed as defined and authorized in the MBRF Trust Agreement;
2. Interact with Executive Director, Trustees and Board Chair, as necessary via print and electronic communications;
3. Interact with MBRF Executive Director, legal counsel and accounting representatives for tax preparation of the 990-PF, 990-T and 1099-MISC;
4. Interact with the personnel of the McKnight Brain Research Institutes, as directed by the MBRF Executive Director;
5. Manage all meeting arrangements, including securing meeting location, arranging for meals, arranging for telephones or audio visual equipment as necessary and making trustee reservations;
6. Travel to and attend Trustee meetings and site visits, as requested;
7. Prepare minutes of Trustee meetings for Executive Director review and submission to the Board Chair;
8. Serve as custodian and provide periodic reports to the Executive Director and Trustees on the inventory of the Foundation records, and maintain the archives for the historical records of the Foundation, located at the Truist offices, 333 S. Garland Avenue, 17th Floor, Orlando, FL 32801;
9. Act as a liaison between the portfolio managers of the Foundation and the Executive Director and legal counsel, for regular reports to the Trustees;
10. Handle capital calls for private equity holdings, and liquidation requests from equity fund managers approved by the portfolio manager;
11. Maintain accounts and disburse payments for the Travel Award Program, Bio-Informatics Core and Neuroimaging Core and Cognitive Aging Test Battery Working Group, and others as authorized by the Executive Director on behalf of the organization;
12. Handle deposits and payments for meeting venues and provide guidance as necessary to support the Executive Director in working with the host institution for the Inter-Institutional Meeting;
13. Handle payment of Trustee compensation, taxes, grant commitments, trustee expense reimbursements, travel award payments, Inter-Institutional meeting participant reimbursements, Executive Director travel reimbursements, and other expense reimbursements, as well as office operational expense payments as required;
14. Handle other Trustee or Executive Director hotel reservations and travel arrangements as necessary and requested by the Trustees and/or Executive Director
15. Perform other responsibilities assigned or delegated by the Board or Executive Director.

Approved November 8, 2017

The McKnight Brain Research Foundation appoints Amy Porter to Executive Director Position

The McKnight Brain Research Foundation (MBRF) is pleased to announce the appointment of Amy McGuire Porter as its Executive Director (ED) effective, April 1, 2018. The ED is the chief management officer of the MBRF and reports directly to the Board of Trustees (Board) through the Chair of the Board. The ED serves as the lead representative of the organization, along with the chair and as its primary spokesperson to all stakeholder groups.

Amy has served as a non-profit professional for over 30 years with 16 years' experience serving as executive director and CEO of two national, health-related organizations – the Foundation for NIH (2001-2010) and the National Osteoporosis Foundation (2010 - 2017).

During Amy's nine-years as Acting and then Executive Director of the Foundation for the National Institutes of Health (FNIH), nearly $500 million in contributed revenue was received and for four consecutive years the FNIH received Charity Navigator's highest 4 Star Ratings. The development of a pioneering form of public-private partnership that produced the Alzheimer's Disease Neuroimaging Initiative and the Biomarkers Consortium, are major achievements under Amy's leadership.

During Amy's tenure at FNIH, the Bill and Melinda Gates Foundation provided $200 million to design, launch and manage Grand Challenges in Global Health, a five-year grant program to foster innovation in solving key global health and development problems. In addition, FNIH managed the Mouse Genome Sequencing Consortium, issuing $24 million in grants to three academic centers, speeding up the determination of the DNA sequence of the mouse genome. Other major programs include the Genetic Association Information Network, a program to genotype existing research studies combining the results with clinical data to create a new resource for genetic researchers; the Edmond J. Safra Family Lodge and Garden on the NIH campus. The Research Partnership in Cognitive Aging, a public-private partnership with the National Institute on Aging and the McKnight Brain Research Foundation to support research on age-related changes in the brain influencing cognition and memory loss associated with normal aging was formed during Amy's tenure at the FNIH

In 2010, Amy became the CEO and Executive Director of the National Osteoporosis Foundation (NOF). In her role, she was the primary spokesperson to all stakeholder groups. She was responsible for overseeing strategic planning, operations, and administration of the organization. Additional duties included identifying and developing educational and research priorities, enhancing the NOF image and enriching all levels of engagement with patients, caregivers, physicians and the public.

In Amy's first year at NOF, she established the National Bone Health Alliance (NBHA) based on the Biomarkers Consortium model developed at FNIH. NOF manages the NBHA, a successful consortium of over fifty-member organizations joining together to advance research, advocacy and education in osteoporosis and rare bone diseases, and promote bone health. NBHA members include other nonprofit organizations, medical societies, pharmaceutical and diagnostic industry partners, and nutrition and exercise companies. The NIH, FDA, NASA and CDC participate as advisors to the NBHA.

Amy has a Bachelor of Art degree from Kent State University and attended the master's in arts administration program at the University of Akron. In 2005, Amy was the recipient of the National Institutes of Health (NIH) Clinical Center Director's Award for her work in support of NIH patients and their families. In 2009, Amy received the Honorary Alumna Award from The University of Akron for her work in support of health and biomedical research. In 2017, Amy received the New Jersey Interagency Council Professional Award and was appointed as a member of the Stakeholder Advisory Committee to the CEO of Pharmaceutical Research Manufacturers of America ((PhRMA).

The purpose of the MBRF is to promote research and investigation of the brain in the fundamental mechanisms that underlie the neurobiology of memory with clinical relevance to the problems of age related memory loss. Amy's background and experience make her uniquely qualified to serve as the MBRF's ED.

Executive Director Goals for 2022-2023

Executive Director Name	Revised and Approved by the Executive Committee
	May 2023

1. Organizational Goals		
Area	**2022-23 Goals to be Reviewed and Approved July/August 2023**	**Results to be Reported June 2023**
Board Development, Membership and Governance	Develop positive and productive relationship with all the Trustees through introductory calls and continued engagement Advance the candidate nomination and recruitment process to add at least two new Trustees to the board in 2023 Develop regular meeting cadence with MBRF Chair to share updates and receive ongoing feedback Proactively schedule committee meetings when appropriate and develop relevant meeting materials	
McKnight Brain Institute Relations	Develop collaborative relationships with the MBIs and work to understand the unique structure & history of each MBI Work with MBIs to support their efforts to seek wider participation in the pilot grant program and enhance awareness of this initiative within MBIs	

	Participate and support the Communications Working Group to ensure consistent meeting schedule and continued collaboration between the communications representatives of the MBIs and the MBRF	
External Partner Relations	Continue to nurture current external partner relationships, understanding the unique history, and shared goals Identify national collaborative networks to engage with other like-minded organizations and increase visibility of the mission and strategic initiatives of the MBRF Identify potential new partners for promotion of MBRF messages and distribution of educational resources Grow the MBRF's network of like-minded organizations and funders to explore synergies and share learnings	
Strategic Development - Education	Develop and implement national search process to identify a consulting firm to complete a landscape analysis and scoping document for the PCP Initiative Work with the consultant to ensure successful completion of the study Develop and share strategic recommendations to the board on how to advance the PCP initiative, based on the completed study Begin implementing board-approved strategy/strategies for the PCP initiative	

Strategic Development - Communications	Implement all components of current communications plan Develop cadence of quarterly tracking and reporting to Trustees on key metrics (web site traffic, social media engagement, etc.) Lead process to develop new communications plan and proposed budget starting July 2023 Continue to highlight the MBI and MBRF activities, events, news and activities on social media and website Increase development of new content for the website that will attract and engage more visitors to McKnightBrain.org Increase audience engagement with MBRF web site, newsletter and social media channels	
Strategic Development – Research	Continue to work closely with funding partners on current research partnerships, programs, scholarships and awards Continue to work with awardees to follow and track progress and outcome(s) Work with research scholarship partners to increase number of applications Strive to improve the review and award process, working with Trustees and partners (ABF and AFAR) Initiate planning and partnership with NIA/FNIH for Cognitive Aging Summit IV	

Finance and Administrative Operations	Continue to monitor with the Corporate Trustee the operations expenses against the current operating budget Continue to monitor funding for the communications plan and related special activities and promotions Monitor budget for Education Landscape Analysis Initiative Continue to monitor with the Corporate Trustee all grant timelines, reports, and expenses Ensure grantee reports are submitted on a timely basis and are reviewed by the Trustees Support the Corporate Trustee and the Trustees in their review of financial and investment reports	

2. Demonstrating Performance Factors to be Completed in July 2023

To what degree did you, the Executive Director, demonstrate the following personal attributes, leadership qualities, and competencies in the past year?

Personal Attribute or Leadership Quality	Action that demonstrates Attribute or Quality	Rating 1 - 4
Serves as Change Agent		
Problem Solving		
Systems Thinking		
Partnership Focus		
Effective Communication		

Ethics and Judgment		

Core Competencies	Action that demonstrates Competency	Rating 1 - 4
Understanding of Nonprofit Governance and Management		
Focus on MBRF Key Priorities and Functions		
Understanding of the MBIs' Structure, Research Focus, and Current Priorities and Needs		
Program Management and Oversight		
Ability to See Opportunity and Assess Risk		

Comments: In what priority areas of performance did you, the Executive Director, excel? In what areas is greater emphasis or more action or effort needed?

3. Summary Assessment for August 2022- August 2023, Next Steps, and Vision for the Organization

Overall performance rating: _____

4 - Exceeds Expectations
3 - Meets Expectations
2 - Partially Meets Expectations
1 – Requires Increase in Emphasis or Effort

Comments to be provided by the Board of Trustees

1. What are 1-3 notable areas of the Executive Director's strength?

2. What are 1-3 areas for greater emphasis and understanding or an increase in activity?

3. What do you see as your vision for the MBRF in the next year? Is your vision reflected in the goals set forward by the Executive Director? If not, please note here.

4. Board Self-Reflection

1. What have you, the Trustees as a whole, done well or effectively to provide support to the Executive Director?

2. What might the Trustees have done differently?

3. As you review the goals for next year, what support is needed from the Trustees to move each area of accountability forward?

4. What goals would you establish for the Board of Trustees for next year?

SpencerStuart

Position and Candidate Specification

McKNIGHT BRAIN RESEARCH FOUNDATION
Preserving memory, enhancing life

Chief Executive Officer

PREPARED BY:
Philip Jaeger
Shannon Yeatman
Kaitlin Hayes

September 2024
Assignment: 66286-001

The McKnight Brain Research Foundation is an Equal Opportunity Employer and encourages candidates of all backgrounds to apply for this position.

About the Foundation

Enhance life by preserving memory and supporting healthy cognitive aging through research and education.

Founded in 1999 by Evelyn F. McKnight, the McKnight Brain Research Foundation is the only private foundation devoted exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health. With cognitive changes due to the normal aging process potentially affecting the majority of people aged 65 and older, the McKnight Brain Research Foundation works to champion research to better understand age-related cognitive decline and memory loss. As leaders in cognitive aging research, the Foundation is also committed to sharing its research findings and practical suggestions for maintaining brain health with the scientific community and the public at large.

Since its founding, the Foundation has established Evelyn F. McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, and the University of Miami, and the Evelyn F. and William L. McKnight Brain Institute at the University of Florida.

By partnering with the Foundation for the National Institutes of Health, and with the support of four National Cognitive Aging Summits and the National Academies Cognitive Aging Report, the McKnight Brain Research Foundation has made great progress toward better understanding the effects of age-related cognitive decline and memory loss over the last two decades. The McKnight Brain Research Foundation will strive to continue promoting advancements in the field of cognitive aging and age-related memory loss through scholarships, research awards, and educational programs to optimize Brain Health.

For more information, please visit the McKnight Brain Research Foundation website.

Values Statement

INTEGRITY

The McKnight Brain Research Foundation conducts its affairs with the highest degree of honesty, integrity, and accountability.

COMMITMENT

We are committed to our vision of helping people optimize a healthy brain throughout life.

DISCOVERY

We value scientific curiosity and discovery leading to clinical interventions in age-related cognitive decline and memory loss.

The McKnight Brain Research Foundation seeks a visionary and strategic leader with fluency in basic and/or clinical neuroscience and related health sciences to lead and advance the Foundation's mission and purpose of preserving memory and supporting healthy cognitive aging through research and education. Fundamentally, the Chief Executive Officer (CEO) will harness the unique elements of the Foundation in order to translate research in cognitive aging to the care and treatment of patients, thereby improving the lives of innumerable individuals and families.

The Foundation benefits from a committed board, strong partnerships with federal funders, and four thriving brain research Institutes at major academic medical centers. The conditions are right to set a scientific agenda and raise visibility to ensure that the Foundation remains a vital driver and contributor to the understanding of age-related cognitive decline and memory loss.

The CEO will be a passionate, collaborative, and driven professional, who will serve as the inaugural chief administrative officer of the Foundation, reporting directly to the McKnight Brain Research Foundation Board of Trustees. Along with the Board Chair, the CEO serves as the lead representative of the organization and primary spokesperson for the Foundation. The CEO is responsible for overseeing all strategic planning, operations, and administration of the organization's programs, finances, marketing, and grant distributions. The CEO is further supported by the Corporate Trustee who has additional duties and works closely with the Foundation.

This role will be fully remote with some travel required to attend Trustee meetings, the annual Inter-Institution Meeting, and additional meetings as directed or approved by the Board.

KEY RELATIONSHIPS

Reports to

Board of Trustees

Other key relationships

Corporate Trustee
Leaders of the four campus-level McKnight Brain Institutes:

- University of Florida
- University of Alabama at Birmingham
- University of Arizona
- University of Miami

National Institutes of Health
National Institute on Aging
American Brain Foundation
American Federation of Aging Research
American Academy of Neurology
Foundation for the National Institutes of Health

IDEAL EXPERIENCE

Mission alignment

Evidenced dedication to advancing healthy cognitive aging through research and education, with an understanding of translational research within the health care and/or academic sectors.

Executive leadership

Significant senior management experience or relevant comparable experience and background; strong organizational planning and delegation skills.

Financial acumen

Fiduciary management experience, including budget preparation, analysis, decision-making, and reporting.

Public relations and communications

Experience serving as the external face of an organization or division, with excellent written and oral communication skills; ideally, exposure to marketing campaigns and strategy.

Stakeholder engagement

Demonstrated ability to lead through influence and engage a wide range of stakeholders.

Advanced degree

An M.D. or Ph.D. or equivalent in education and training in a relevant field such as medicine, neurosciences, public health, basic and life sciences, from a recognized university accredited through the U.S. Department of Education and the Council on Higher Education.

Serving on and/or reporting to a board

CRITICAL LEADERSHIP CAPABILITIES

Strategic & Visionary Mindset

The CEO will be a strategic thinker who will provide dynamic leadership in charting the future for the Foundation. In doing so, the CEO will:

- Create and implement a programmatic strategy that better links and articulates the progress of the grantees in meeting the strategic goals of the Foundation.
- Contribute to the development of a strategic plan and new initiatives based on a broad understanding of the health and academic sectors, as well as age-related cognitive health issues.
- Track and communicate the trends and shifts occurring in the health care ecosystem that potentially pose challenges to the Foundation's mission.

Driving Results

The McKnight Brain Research Foundation is the nation's only private foundation dedicated exclusively to solving the mysteries of the aging brain, particularly age-related cognitive decline and memory loss. The CEO is expected to expand recognition of the organization and:

- Pursue new initiatives and strategic partnerships to further the goals and priorities of the Foundation.
- Maintain awareness of the challenges and opportunities for its grantees and partners, adjusting the programmatic strategy as needed in concert with the Board.
- Identify areas where the Foundation and its related Institutes can have significant influence.

External Representation

As the chief ambassador for the Foundation, the CEO will:

- Champion a compelling vision and purpose, effectively engaging and influencing other leaders from neuroscience research, education, and professional communities.
- Build innovative and distinctive partnerships and alliances across the field to increase the Foundation's influence and profile, thereby broadening the impact of the Foundation's goals, vision, mission and work.
- Catalyze crucial dialogue with leaders across the health care sector and related communities—ultimately, helping to establish age-related cognitive aging and memory concerns as a standard part of brain health maintenance.

KEY RESPONSIBILITIES

- Report to and work closely with the Foundation Board, regularly communicating with the Board Chair and Trustees to provide updates, seek the Board's involvement in policy decisions, ensuring that the organization's mission is represented in its strategic planning goals.
- In concert with the Board Chair, ensure good governance and Board engagement; develop, maintain, and support a strong board; serve as ex-officio of each committee.
- Convey the vision of the Foundation's strategic future to, actively engaging and energizing, the Board, the four McKnight Brain Institutes, and other external stakeholders—including the National Institute on Aging, Foundation for the National Institutes of Health, American Brain Foundation, American Federation of Aging Research, and the American Academy of Neurology, and any future partners.
- Ensure operational excellence in administration, finance, grantmaking and program evaluation, communications, and Board support, including all systems and resources needed to achieve strategic goals, ensuring maximum resource utilization, and maintaining a positive financial position.
- Oversee the execution of a programmatic and grantmaking strategy that adheres to the Foundation's mission, ensure effective systems to track progress, regularly evaluate program components, and communicate status of successes to the Board, the Institutes, and other stakeholders.
- Establish a strong relationship of support and provide guidance to the leadership of the four McKnight Brain Institutes.
- Maintain relationships with grantees, other funders of similar research, and leaders at each grant site, while increasing the overall visibility of the Foundation throughout the sector; leverage external presence and relationships to garner new opportunities for collaborative funding and build national recognition for the importance of age-related cognitive decline and memory loss.

- Be active and visible in identified relevant sectors and communities, advancing the Foundation's mission and its brand as the recognized leader in supporting clinical translational research in age-related cognitive decline and memory loss—in contrast to other neurogenerative diseases—from research laboratory to clinical practice.
- Expand existing partnerships, forging collaborations with various organizations throughout the brain/neuroscience research community, the medical, clinical research, and academic spaces, relevant training organizations, and public and private organizations related to the Foundation's mission.
- Serve as one of the Foundation's primary spokespersons internally and externally, representing the Board and organization at grantee site visits, meetings with professional partners and other stakeholders, as well as to organizational constituents, the media, and the general public.
- Coordinate with the Corporate Trustee, serving as the primary liaison between the Corporate Trustee and the Board.
- Collaborate with existing consultants to deepen and refine the branding and marketing strategy—from web presence, social media, and trade media to external relations—with the goal of creating a stronger brand for the Foundation.
- Work diligently with health care educators to convey the importance of including cognitive aging and memory loss in educational programs and seek additional pathways to expand research in the discipline.
- Actively engage health care practitioners to further efforts around the inclusion of cognitive assessment as a standard of care and component of health maintenance.
- Advise the Board on organizational structure, with the potential to establish internal staff roles at the Board's discretion; establish employment and administrative policies and procedures for all day-to-day operations and functions of the Foundation.
- Improve the annual review process across the four McKnight Brain Institutes, ensuring transparent communication, more timely reporting, and better adherence to the mission of the Foundation.
- Assist the Board in determining the appropriate approval levels for the CEO role in order to streamline grant and fiduciary approval processes.

OTHER PERSONAL CHARACTERISTICS

- Resilient, adaptable, and nimble
- Humble and empathetic, with high EQ
- Optimistic, collegial, and transparent
- Entrepreneurial and innovative
- Strategic thinker
- Curious
- Authentic relationship builder
- Integrity

COMPENSATION

The base salary range for the Chief Executive Officer position will be $200,000 - $300,000 per year, commensurate with experience and qualifications, or as mandated by a U.S. Department of Labor prevailing wage determination. Other compensation associated with this position may include administrative salary supplement and allowances. The McKnight Brain Research Foundation is an equal opportunity employer and encourages all qualified applicants to apply.

APPLICATION

The Foundation has retained Spencer Stuart to support this search. If you wish to submit your own application or nominate someone to serve as the next CEO, please send an email message with supporting materials to McKnightBrain@SpencerStuart.com.

Alice H. Luo Clayton, Ph.D.

alice.clayton716@gmail.com
Princeton Junction, NJ 08550

SUMMARY

I am a Ph.D.-trained systems neuroscientist dedicated to advancing scientific knowledge toward improving the human condition. With nearly **15 years of programmatic leadership and strategic advising in government and private philanthropy**, I keenly understand the research ecosystem's opportunities and challenges. My expertise spans basic, translational, and clinical research, where I thrive on bringing diverse together perspectives toward common goals. **My passion is connecting the dots into new shapes that lead to innovative and pragmatic solutions for unmet needs.**

EXPERIENCE

SENIOR SCIENCE ADVISOR, NATIONAL INSTITUTES OF HEALTH (NIH), BRAIN RESEARCH THROUGH ADVANCING INNOVATIVE NEUROTECHNOLOGIES® (BRAIN) INITIATIVE

2023 - Present
Office of the BRAIN Initiative Director (OBD)

- **Lead a developing strategic effort** to map the scientific future of the NIH BRAIN Initiative, a program that has transformed neuroscience research by investing over $3B in technology platforms, resources, and foundational knowledge in its first 10 years.

- **Nurture scientific coordination** among NIH Institutes/Centers, federal partners, and external organizations to support integrative efforts across the BRAIN Initiative.

SENIOR PROGRAM DIRECTOR

2022 - 2023
Coalition for Aligning Science (CAS)

- **Spearheaded the initial strategic roadmap for a new initiative supported by the Sergey Brin Family Foundation (SBFF).** Our green-lit recommendation report leveraged my deep subject matter expertise in autism research and distilled landscaping interviews with 70+ key opinion leaders.

- **Authored an authoritative report on the state of autism science,** identifying cross-cutting scientific and organizational challenges, and posing actionable solutions for step-change progress across basic, translational, clinical, and implementation science.

SENIOR SCIENTIST

2011- 2022
Simons Foundation Autism Research Initiative (SFARI)

- **Served as primary scientific liaison for the Simons Foundation Initiative for the Developing Brain (SIDB)**, an over $50M commitment to support 40+ Principal Investigators at the University of Edinburgh, Scotland.

- **Oversaw SFARI's preclinical efforts** in a potential small molecule therapeutic for which the Simons Foundation held the FDA IND. My efforts directly led to the initiation 16hthouse study, an ongoing clinical trial to examine the therapeutic efficacy of arbaclofen for human carriers of 16p11.2 deletion genetic syndrome.

- **Served as the senior leader of the multi-year, milestone-driven partnership** with F. Hoffmann-La Roche Ltd to develop and manage a high throughput behavioral screening of multiple mouse models of autism.

- **Conceived and oversaw the SFARI Autism Rat Consortium**, a $10.2M international research collaborative aimed at uncovering the systems, behavioral, and social mechanisms underlying autism.

- **Spearheaded the Human Cognitive and Behavioral Science funding program** which leveraged the flourishing advances in cognitive neuroscience, computer science, and engineering to improve the quantitative understanding of neurobehavioral phenotypes across the autism spectrum.

- **Created and managed the Bridge to Independence (BTI) program**, a prestigious award that prioritized inclusive excellence and provided critical funds and wrap-around professional development support.

- **Served as the scientific manager of the systems neuroscience grant portfolio**, which spanned animal neural circuits to human cognitive neuroscience grants. I was the programmatic driver in the expansion and development of this portfolio from approximately $6M in 2011 to over $33M in 2022.

AAAS SCIENCE & TECHNOLOGY POLICY FELLOW

2009 - 2011
National Institute of Mental Health (NIMH)

- **Served as an integral programmatic member of the Human Connectome Project (HCP)**, a $39M effort that ushered in a new era of human neuroimaging research.

- **Oversaw peer review of an RFP contract solicitation** to create a clinical trials network for testing novel, rapidly-acting interventions for treatment-resistant depression (TRD). The resulting network was pivotal in achieving FDA approval of ketamine-based drugs for TRD.

- **Lead programmatic management of a NIMH grant portfolio** focused on longitudinal pediatric cohorts for anxiety and trauma-based disorders.

EDUCATION

Postdoctoral Intramural Research Training Fellow
2007-2009
National Institute on Drug Abuse, Baltimore MD

Doctor of Philosophy, Neuroscience
2001-2007
University of Pennsylvania, Philadelphia PA

Bachelor of Arts, Psychology; Minor, Zoology; summa cum laude
1995-2000
North Carolina State University, Raleigh NC

SELECTED SCIENTIFIC REVIEW SERVICE

Invited Member, Grants Workgroup
2024
California Institute for Regenerative Medicine (CIRM)

- Invited to peer review grant applications for their new ReMIND program, which provides up to $8M per award to conduct large-scale, collaborative research on neuropsychiatric disorders.

SELECTED PEER-REVIEWED PUBLICATIONS

- Kabitzke P.A., Brunner D., He D., Fazio P.A., Cox K., Sutphen J., Thiede L., Sabath E., Hanania T., Alexandrov V., Rasmusson R., Spooren W., Ghosh A., Feliciano P., Biemans B., Benedetti M., **Luo Clayton A** (2018). Comprehensive analysis of two Shank3 and the Cacna1c mouse models of autism spectrum disorder. *Genes Brain Behavior*, 17, 4-22.

- **Luo, A.H.**, Tahsili-Fahadan, P., Wise, R.A., Lupica, C.R., Aston-Jones, G (2011). Linking Context with Reward: A Functional Circuit from Hippocampal CA3 to Ventral Tegmental Area. *Science*, 333, 353-357. *Also listed as the corresponding author.*

Board of Trustees
Reorganization Summary
And
MBRF Priority Areas

Board of Trustees Reorganization Summary
And Priorities for 2020 – 2023

Since its inception in 1999, the McKnight Brain Research Foundation (MBRF) was managed by consensus of the three founding trustees. Founding Trustee, Dr. Lee Dockery, served as the primary coordinator and manager. However, upon the establishment of the four McKnight Brain Institutes, the trustees felt the need for additional assistance in reviewing progress and making site visits. A fourth trustee was added in 2006 and a fifth in 2009. Currently there are six trustees in addition to the Coprorate Trustee and Chair Emeritus serving. A maximum of eleven trustees are allowed in the MBRF's Trust documents.

The duties and responsibilities of each trustee were developed and approved in 2015. A Chair and Vice Chair were elected in 2015. At the strategic planning meeting in 2017, it was reaffirmed by the trustees that the MBRF would continue in perpetuity. In doing so, the MBRF committed to becoming a more public-facing organization. With Dr. Lee Dockery's announcement of his intention to retire in 2019, the trustees voted establish a part-time Executive Director position who would become the Chief Administrative Officer of the MBRF. After a successful national search, Amy Porter accepted the offer and became the first Executive Director in April 2018.

With the impending retirement of Dr. Lee Dockery as MBRF Chair, the trustees recognized the need for enhanced individual and collective participation by the trustees. The justification and plan for reorganization were approved by the Board of Trustees at its meeting on October 30, 2018. The approved reorganization plan created an operational board structure composed of the Chair, Vice Chair, the Chairs of five new standing committees, the Executive Director, Corporate Trustee and the Chair Emeritus.

The five approved standing committees are:

1. Communications
2. Education
3. Finance
4. Membership and Governance
5. Research

As an outcome of the reorganization of the Board of Trustees, programs in Communications, Educations and Research were identified as priority areas of growth and development by the MBRF for 2020-2023.

The charters for each of the committees were approved by the Board of Trustees on February 20, 2019, and are included for review and information. The list of members of the committees is also included. It is hoped that each MBRF Trustee participates on at least two committees upon invitation by the MBRF Chair.

Included in the charters of the Communications, Education, and Research Committees are provisions for non-trustee advisory members to be appointed to those three committees. The advisory members provide expertise in committee priority areas. Criteria for appointment of advisory members is included in this section.

With the establishment of standing committees, the MBRF is able to assign responsibility for implementation and oversight of the three priority programs.

1. Communications Committee
   Chair: Richard I Isaacson, MD
   Purpose and Powers: See Charter

A. Summary of Activity

- Appointed Valerie Patmintra Senior Communications Advisor (Bio attached).
- Convened Communications Working Group meeting.
  (See Attached Charter and Working Group Membership Attached).
- A two-year communications plan with a budget not to exceed $300,000
  (See attached prospectus).
- Endorsed Key Messages statement on cognitive aging, Cognitive Decline, and Memory Loss developed by the communication working group. (See Attached).
- Produced a short video commemoration of the 20-year history of the MBRF and was shown at the April 10, 2019, Inter- institutional Meeting. The video resides on the MBRF website.
- First Communications Workshop was held in connection with the 11th Inter-Institutional meeting (April featuring a panel discussion on the importance of Communication of the science surrounding age related cognitive decline and memory loss.
- The newly developed and redesigned MBRF website was launched including individual MBI website content and links to between each other of the individual MBI websites.
- Trustees previewed first draft of MBRF/MBI organizational brochure describing the organizational relationship between the MBRF and each of the MBIs as well as individual profiles of each MBI.
- Approval of a link from the MBRF website to MindCrowd website. MindCrowd is a web-based memory study designed to analyze how genetics influences memory. Participants age 18 or older are invited to take a 10-minute online test. It was thought individuals visiting the MBRF website would benefit from the additional information on age-related cognitive decline and memory loss on the MindCrowd website and could contribute to the research finding by taking the examination. For more information, visit www.mindcrowd.org.
- Developed a social media initiative through Twitter and LinkedIn to share info from MBRF and the MBIs. Articles and events are posted to the Twitter feed regularly. The new MBRF logo is in use on Twitter.

B. Goals for 2020-2021

- Continue to buildout website and content development development.
- Continue development of organizational brochure.
- Produce and upload organizational brochure.
- Continue to grow the collaborative relationship with the MBIs through the communications working group.

- **<u>Board Approved Priority</u> -- Proceed with efforts to build the audience for the MBRF website and social media platforms. Develop strategies to reach Primary Care Physicians (PCPs) as a target audience. (Audience Building Plan included with this document.)**

2. Education Committee
   Chair: Robert Wah, MD
   Purpose and Powers: See Charter

A. Summary of Activity

The Education Committee (with the Research Committee) reviews content before it is posted on website, published, or included in print materials or slide presentations, ensuring consistency with key messages. The committee reviews for accuracy, soundness, and alignment with the MBRF mission, current scientific understanding, and clinical practice.

- Develop and curate website content addressed to individuals, families and caregivers of those with age-related cognitive decline and memory loss.
- Develop and curate website content developed for individuals on how to protect, maintain brain health.
- Develop brochure copy to raise awareness and promote the MBIs and MBRF to individuals, partners, donors.
- The Annual Inter-Institutional Meeting between the four MBIs has served to identify educational opportunities and implement activities inspiring commitment and shared vision.
  The 12th Inter-institutional meeting scheduled for April 2020 was cancelled due to the pandemic and has been rescheduled for April 2021, although this date may be adjusted to the fall of 2021.
- The McKnight Scholars will be invited to the 2021 Inter-Institutional Meeting to meet the researchers at the MBIs and for the graduating scholars to present on their research.
- The Annual William G. Luttge Annual Lectureship in Neuroscience at the University of Florida is presented by a research scientist of national or international prestige in the field of neurosciences. The Lectureship was established in 2012, honoring the Founding Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida. Lectureship value--$250,000; Expense Fund--$50,000 for immediate inauguration of the Lectureship.

- **<u>Board Approved Priority</u> – Identify, develop, and disseminate educational content for Primary Care Physicians (PCPs) as a much-needed resource in their practices. (See PCP Content Outline included with this document.)**

3. Research Committee
   Chair: Madhav Thambisetty, MD, PhD.
   Purpose and Powers: See attached Charter
   A. Summary of Activity
   - Appointed Dr. Robert Krikorian as the first advisory member to a committee after the reorganization of the Board of Trustees in October 2018. Dr. Kirkorian is Professor of Psychiatry and Behavioral Neuroscience at the University of Cincinnati Health Center.
   - Reviewed and revised, in collaboration with the finance committee, the template for the MBI Annual Report to the MBRF to make it easier to read and evaluate.
   - Approved a request from the MBI at UM for $200,000 for pilot funding over two years to establish a Neurocognitive Post-Doctoral Clinical Fellowship to begin July 1, 2020.
   - Approved a request from the MBI at UA for $244,400 for participation in the Precision Aging Demonstration Pilot by its partner MBI at UM to provide additional cohort sample data requested by the NIH following preliminary review.
   - Reviewed and approved two Inter-Institutional grant proposals recommended for funding by the Cognitive Aging and Memory Intervention Core Committee.

     1. Vulnerability of Older Adults to Financial Deception Schemes—A Novel Intervention Tool--$60,000 per year for two years.

     2. A pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults. --$60,000 per year for two years.

     3. Transcutaneous Vagal Nerve Stimulation and Cognitive Training $60,000 per year for two years.

- Reviewed and recommended renewal of the Research Partnership in Cognitive Aging with the National Institute of Aging (NIA) through the Foundation for NIH for the third five-year cycle to begin in Spring of 2020 (Postponed until Spring 2021), (1st cycle-2009, 2nd cycle 2014, 3rd cycle approved 2019). It is expected the MBRF will fund $1 million per year for five years and will be matched by the NIA at $2 million year for five years.
- Approved the request to fund the Reserve & Resilience Workshop Pilot Grants Project for 2020. The MBRF supported the 2019 workshop for $30,000 at which there were over 300 Attendees (8 MBI researchers). The National Workshop on Cognitive Reserve and Resilience is an outcome of Cognitive Aging Summit III funded by the MBRF with the NIA through the FNIH.
- Reviewed and recommended for funding two McKnight Brain Research Foundation Clinical Translational Research Scholarships through the American Academy of Neurology (AAN) and American Brain Foundation (ABF). Each scholarship award is for $150,000 for the two-year period. The 2020 McKnight Scholars is third cycle of for the scholarships.
- The MBRF hosts an Annual Poster Reception in conjunction with the Annual Meeting of Society for Neuroscience (SfN). The annual meeting scheduled for October 24 – 28, 2020 was cancelled. The 2019 Poster Reception had 70 posters submitted and were judged By Dr. Molly Wagster and Dr. Jon King from the NIA. Cash awards were made for 1st, 2nd and 3rd place plus three honorable mention awards.
- In collaboration with the education committee, approved Content Outline for PCPs' area of the McKnightBrain.org Website and resources to be added to the McKnightBrain.org website to support the educational initiative targeting PCPs. (See attached Content Outline for PCPs).
- In collaboration with the communication, education committees, approval of a link from the MBRF website to MindCrowd website., MindCrowd is a web-based memory study designed to analyze how genetics influences memory. It was thought individuals visiting the MBRF website would benefit from the additional information on age related cognitive decline and memory loss on the MindCrowd Website and could contribute to the research finding by taking the examination. For more information, visit www.mindcrowd.org.

- **<u>Board Approved Priority</u> - The Research Committee developed a proposal to establish the McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss with the following commitments:**
  - **a. Length of award: three years, renewal annually after satisfactory review.**
  - **b. Amount of Award: $250,000 per year with match from the host institution.**
  - **c. The Foundation commits to funding the program for a five-year initial trial period which would have supported 12 scientists at the conclusion of the five-year cycle.**

  The Research Committee developed a prospectus describing the McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss suitable to distribute to potential partners to jointly sponsor and fund the mid- career research awards. (See Prospectus).

McKnight Brain Research Foundation

Charter of the Membership and Governance Committee

of the Board of Trustees

Purpose

The Membership and Governance Committee shall coordinate the Board of Trustees' oversight responsibilities by periodically reviewing Board composition and by identifying, recruiting, and recommending candidates for appointment, or re-election of current Trustees, consistent with applicable qualifications required by the April 6, 2015, document "Board Member Duties and Responsibilities." The Committee shall review periodically, or as requested by the Chair of the Board, the succession process for officers of the Board. The Committee shall oversee annual board self-evaluations, Trustee orientation and training, and will periodically review and make recommendations on Board size, committee structure, charters, policies, process, and practices of the Board and its Committees. The Committee shall recommend to the Board the establishment of special committees and advisory councils. The Membership and Governance Committee reports to the Board of Trustees.

Members

The Chair of the McKnight Brain Research Foundation (MBRF) Board of Trustees shall appoint a Membership and Governance Committee, consisting of no fewer than two (2) members, inclusive of the Chair of the Committee. The Chair of the Board of Trustees shall serve as non-voting, ex officio member. The Executive Director shall serve as a non-voting, ex officio member. All members shall be MBRF Trustees.

Meetings

The Membership and Governance Committee shall meet at those times and places as determined by the Chairman of the Membership and Governance Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Committee shall recommend to the Board of Trustees candidates for appointment and re-election as Trustees. These candidates shall demonstrate knowledge, passion and commitment to the mission of the McKnight Brain Research Foundation, as well as sound judgment and a willingness to act collaboratively. The Committee shall periodically review Board composition for the appropriate balance of expertise, specialty, size, structure, and diversity and make recommendations to the Board of Trustees. The Committee shall develop orientation material and participate in the orientation and training of new Trustees. The Committee shall review Trustee self-assessment tools and make recommendations to encourage 100% participation. The Committee shall periodically review the charters of all Board Committees and recommend to the Board of Trustees any changes and additional committees or advisory councils to be established. The Committee shall perform such other duties as may from time to time be required by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation

Charter of the Finance Committee

of the Board of Trustees

Purpose

The Finance Committee shall coordinate the Board of Trustees' financial oversight responsibilities. The Committee shall be responsible for the planning, monitoring, and evaluation of the McKnight Brain Research Foundation's (MBRF) policies and programs for funding, financial management, assets, risks, and insurance. The Finance Committee reports to the Board of Trustees.

Members

The Chair of the McKnight Brain Research Foundation Board of Trustees shall appoint a Finance Committee, consisting of no fewer than three (3) members, inclusive of the Corporate Trustee, and the Chair of the Finance Committee, and at least one (1) other Trustee. The Chair of the Board of Trustees shall serve as non-voting, ex officio member. The Executive Director shall serve as a non-voting, ex officio member.

Meetings

The Finance Committee shall meet at those times and places as determined by the Chair of the Finance Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Finance Committee monitors MBRF's financial records; reviews and oversees the creation of accurate, timely, and meaningful financial statements to be presented to the Board of Trustees; reviews annual MBRF operating expenses; reviews financial reporting from McKnight Brain Institutes (MBIs); anticipates financial risks; monitors and ensures safeguarding of MBRF assets; monitors compliance with federal, state, and other financial reporting requirements; ensures adequacy of MBRF internal controls and compliance with conflicts of interest policy and other code of conduct policies; and advises the Trustees on the status of the MBRF's finances, and those reported by the MBIs. The Finance Committee works with the Corporate Trustee, the Investment Manager, the Chair of the Board of Trustees, and the Executive Director to develop long range financial planning. The Committee shall perform such other duties as may from time to time be required by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation

Charter of the Communications Committee

of the Board of Trustees

Purpose

The Communications Committee shall provide strategic direction to the communications programs to ensure effective communication of the McKnight Brain Research Foundation's (MBRF) mission, initiatives, and programs, and to evaluate the effectiveness of strategies for raising the profile of the MBRF and the McKnight Brain Institutes (MBIs). The Communications Committee shall identify opportunities and implement activities to foster greater public awareness of cognitive aging and age-related cognitive decline and age-related memory loss (which are distinct from pathologic disease states, such as Alzheimer's disease and related dementias.) The Communications Committee reports to the Board of Trustees.

Members

The Chair of the Board shall appoint a Communications Committee, consisting of no fewer than three (3) members, inclusive of the Chair of the Communications Committee and at least two other Trustees. The Chairman of the Board shall serve as non-voting, ex officio member. The Committee may include other non-Trustee persons whose experience in social media, public relations, publications, marketing, and may assist the Committee and the Board of Trustees in the role of spokespersons. The Executive Director shall serve as non-voting, ex officio member.

Meetings

The Communications Committee shall meet at those times and places as determined by the Chair of the Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Communications Committee shall provide oversight and guidance on the communications activities promoting the work of the MBRF, inclusive of its partnerships, educational programs and scientific research. The Committee shall provide oversight on reaching the goals of the approved Communications Plan, review and approve development of future Communications Plans, as well as branding strategies, national awareness campaigns, website development and maintenance, and social media strategies developed by the MBRF. The Committee will seek information and recommendations from the MBRF/MBI Communications Working Group (an inter-institutional group) to promote activities and research at the McKnight Brain Institutes, attendance at inter-institutional meetings and events, and generate interest in scholarship and core grant opportunities. The Communications Committee will periodically review the goals, strategies, marketing plans, and implementation of communications efforts. The Committee will monitor progress on the communications plan and timeline, and will advise the Trustees on the progress to date and make recommendations and request Trustee involvement.

The Communications Committee shall work with the Chair of the Board of Trustees and the Executive Director to develop future Communications Plans and Timelines, and shall perform such other duties as may from time to time be required and approved by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation

Charter of the Education Committee

of the Board of Trustees

Purpose

The Education Committee shall lead efforts to inform the public, the scientific community, health policy agencies, health professional schools, professional societies, and the media on the prevalence and impact of age-related cognitive decline and memory loss, differentiating this natural process from Alzheimer's disease and other dementias.

The Committee shall develop information and resources to assist those living with cognitive decline and age-related memory loss and their family members to better understand, address, and manage cognitive changes and the effect and impact on their lives. The Education Committee shall develop and disseminate information to the public on activities and behaviors that can maintain cognitive health throughout life and help delay or minimize the negative effects of cognitive aging.

The Education Committee shall identify educational opportunities and implement activities among the scientific community to foster greater interest and investment, and to inspire commitment and shared vision in the understanding and alleviation of cognitive aging and age-related cognitive decline and memory loss. The Education Committee shall encourage and endorse educational programs at each of the McKnight Brain Institutes (MBIs) by providing direction, focus and guidance using consistent information and key messages on cognitive aging, age-related cognitive decline and age-related memory loss.

The Education Committee shall work to elevate the importance of age-related cognitive decline and memory loss on the national agenda and shall encourage its inclusion in health professional education curricula, accreditation, examination, and licensing, as well as encouraging greater investment in research and education by federal health agencies. The Education Committee reports to the Board of Trustees.

Members

The Chair of the Board shall appoint an Education Committee, consisting of no fewer than three (3) members, inclusive of the Chair of the Education Committee and at least two other Trustees. Because the Committee is required to make substantive judgments about the content and quality of educational programs, targeting a varied audience and utilizing a variety of delivery methods, the committee may include other non-Trustee members. The Chair of the Board shall serve as non-voting, ex officio member. The Executive Director shall serve as non-voting, ex officio member.

Meetings

The Education Committee shall meet at those times and places as determined by the Chair of the Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

Powers

The Education Committee shall provide oversight and guidance on education activities, inclusive of its partnerships and programs, and assist in plans for the annual Inter-institutional meeting. The Committee shall review and approve all educational materials distributed under the auspices of the MBRF.

The Committee shall share information about scholarship opportunities, panel and presentation opportunities, poster sessions, conference participation, and educational partnerships with nonprofit organizations and health policy agencies and encourage McKnight Brain Research Foundation (MBRF) Trustee and MBI participation.

The Education Committee shall encourage health professional schools, professional societies, and public and private health care organizations to develop and disseminate core competencies, curricula, and continuing education opportunities that focus on cognitive aging as distinct from clinical syndromes and diseases. The Committee shall encourage that cognitive health should be promoted during regular medical and wellness visits for people of all ages.

The Education Committee shall work with the Chair of the Board of Trustees and the Executive Director to develop long range plans, and shall perform such other duties as may from time to time be required and approved by the Board of Trustees.

McKnight Brain Research Foundation

Charter of the Research Committee

of the Board of Trustees

Purpose

The Research Committee shall encourage and assess research at the McKnight Brain Institutes (MBIs) by providing direction, focus and guidance for research that supports the McKnight Brain Research Foundation's (MBRF) mission to investigate cognitive aging, age-related cognitive decline and age-related memory loss (unrelated to Alzheimer's disease or other dementias). The Research Committee shall identify opportunities to promote and implement activities among the scientific community to foster greater interest in cognitive aging and age-related cognitive decline and memory loss. The Committee, by their example and leadership, shall encourage young investigators in this area of research. The Research Committee reports to the Board of Trustees.

Members

The Chair of the Board shall appoint a Research Committee, consisting of no fewer than three (3) members, inclusive of the Chair of the Research Committee and at least two other Trustees. Because the Committee is required to make substantive judgments about the quality of research studies and protocols, familiarity with research is the single most important criterion for service on the committee. The Chair of the Board shall serve as non-voting, ex officio member. The Committee may include other non-Trustee persons. The Executive Director shall serve as non-voting, ex officio member.

Meetings

The Research Committee shall meet at those times and places as determined by the Chair of the Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Research Committee shall provide oversight and guidance on research activities, inclusive of its partnerships and programs. The Research Committee shall review all requests, proposals and applications for funding of research or scholarships. The Research Committee makes recommendations on the merits and limitations of these requests to the MBRF Board of Trustees and may offer adjustments to the study protocol to allow for alignment with the MBRF mission. The Committee shall review and approve for recommendation the objectives and methods of study designs. The Committee will seek information and recommendations from the Cognitive Aging and Memory Interventional Core Committee and the MBRF Leadership Council and MBI Directors. The Committee will monitor progress on funded research studies, and will advise the Trustees and make recommendations.

The Research Committee shall work with the Chair of the Board of Trustees and the Executive Director to develop long range plans, and shall perform such other duties as may from time to time be required and approved by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation
Board of Trustees
Committees and Members

April 2025

Membership and Governance Committee

Susan L. Pekarske, MD, Chair
Melanie A. Cianciotto
J. Lee Dockery, MD
Michael L. Dockery, MD
Madhav Thambisetty, MD, PhD

Finance Committee

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Education Committee

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Patricia Boyle, PhD
Allison Brashear, MD, MBA
Sharon A. Brangman, MD, FACP, AGSF
Roy H. Hamilton, MD, MS, FAAN, FANA, FCPP
Michael L. Dockery, MD

Research Committee

Madhav Thambisetty, MD, PhD, Chair
Patricia Boyle, PhD
Michael L. Dockery, MD
Roy H. Hamilton, MD, MS, FAAN, FANA, FCPP
Susan L. Pekarske, MD

McKnight Brain Research Foundation
Qualifications for Advisory Committee Members

1. The Board of Trustees of the McKnight Brain Research Foundation (MBRF) has approved non-trustee appointments for membership on three (3) of the MBRF board committees. These committees are the Communications Committee, the Education Committee, and the Research Committee.

2. Trustees serving on committees shall be referred to as "Trustee Members." Non-trustee members of committees shall be referred to as "Advisory Members." Advisory Members serve in a volunteer capacity and receive no compensation.

3. Advisory Members will support the Mission and Purpose of the MBRF by having the experience, education and qualifications to advance the specific goals and activities of the Committee to which they are appointed.

4. Advisory Members are appointed by the Committee Chair. Members serve one (1) year terms, renewable three (3) times, at the Chair's discretion. Advisory Members may serve on more than one (1) Committee, or may be appointed to another Committee at the end of her or his term.

5. An Advisory Member may be invited by the Board of Trustees to attend MBRF meetings, conferences, and events. Invitations will be extended from the Chair of the Board of Trustees. Travel and other expenses related to attending will be reimbursed.

6. Advisory Members must be committed to the Values, Vision, Mission and Code of Ethics of the McKnight Brain Research Foundation.

MBRF Program Priority Areas
2020 – 2023

Communications – Audience Building Plan

Education –Outline of Primary Care Physician Content for mcknightbrain.org

Research – Mid-Career Research Award in Cognitive Aging and Memory Loss

MBRF Program Priority Areas
2020– 2026

1. **Communications** – Audience Building Plan
2. **Education** –Outline of Primary Care Physician Content for mcknightbrain.org
3. **Research** – Mid-Career Research Award in Cognitive Aging and Memory Loss

Overview:

The reorganization of the MBRF and development of priorities for 2020-2023 were established following the MBRF strategic plan approved and reaffirmed in 2017. Since 2020, the MBRF has undergone a lot of changes in its organizational structure with the retirement of two trustees and the appointment of five new trustees. Additionally, Amy Porter, the first executive director (part-time) appointed in 2018 announced her intention to retire following a period of orientation for a new executive director to be recruited. The new executive director was appointed August 15, 2022, and Amy Porter officially retired October 1, 2022.

As a result of these many changes within the organization structure and function it was important to review the Mission and Purpose of the MBRF and the strategic plan for achieving its goals and objectives. With the assistance of a facilitator, the new strategic plan was adopted on October 23, 2023, and the MBRF reaffirmed its Mission, "*To enhance life by preserving memory and supporting healthy cognitive aging through research and education*".

With the approval of the strategic plan the tools of Communication, Education and Research were reaffirmed as priority importance.

In the following pages under sections 8.d. and 9, the historical development of the programs will be listed as well as the current status of each of the priority areas.

With the adoption of the priority areas, it is thought the services of a Chief Executive Officer (CEO) with a scientific foundation and background would be qualified to advance the mission of the MBRF within the scientific and research communities. Therefore, the executive director position was abolished August 15, 2024. The MBRF is grateful to Amy Porter for returning to her position as interim executive director while the search for the CEO position is completed.

McKnightBrain.org Audience Building Plan

I. Attracting General Site Visitors

- **Blogging/Guest Blogging**
  - Adding a blog feature to the website with monthly blogs posted by MBRF Board members, MBI scientists and experts from partner organizations will help boost search results and keep the site fresh with new content
  - Blogs can be tied to new research, current events or commenting on outside science and research to keep ideas fresh each month
  - Guest blogging on partner organization and medical magazine sites can help attract new audiences and drive traffic back to McKnightBrain.org

- **Key Words and Search Engine Optimization**
  - **Build relevancy:** Analyze common words people search for in the field – from general terms like brain health to specific terms and phrases like age-related memory loss and cognitive decline and make sure the site is optimized to use these terms consistently. When site content matches what people search for, it boosts relevancy and increases presence across search engines.
  - **Become an Authority:** The more other sites link to McKnightBrain.org will also help build a presence on Google and other search engines. Look for opportunities where partner organizations can link back to McKnightBrain.org as the authority on age-related memory loss and cognitive decline. Make sure McKnightBrain.org is featured on and linked from all of the MBI websites, reach out to FNIH, NIH, NIA and other partner groups letting them know about the new site and asking for links to our content as appropriate.

- **Build a Social Presence**
  - Leverage Facebook and Twitter to share curated content and drive traffic consistently back to McKnightBrain.org
  - Create a monthly content calendar of posts to share site content, tips and advice, as well as news and information from the MBIs and other partner organizations
  - Link posts back to the website

- **Paid Digital Advertising**
  - **Run a paid Google search ad campaign:** Identify key words and set a budget to reach a daily maximum spend based on clicks or set a max spend for the life of the campaign. With Google, you only pay for clicks through to the website and ads appear when people search for the key words we select.
  - **Facebook ads:** Using a single image or short video clip, you can create Facebook ads to help build an audience for the website as well as build followers on Facebook. With highly customizable demographics, you can target people with specific interests or by age, sex, etc. to increase social and website engagement.

- **Display advertising:** Create visual banner ads to appear on other sites based on individual's interests.
- **Email Marketing:** Purchase targeted email lists and send newsletters, seasonal emails, and/or emails to announce events, awards, scholarship opportunities with links driving back to the website.

II. Leveraging New Awards Program and Primary Care Physician Content to Attract Targeted Audiences

1. Announcing and Driving Traffic to the New Mid-Career Research Awards Program

- **Leverage Social Networks**
  - Draft scheduled social media posts announcing award program, highlighting key dates, profiling awardees and encouraging applications
  - Launch a Facebook ad campaign targeting midcareer researchers – campaign budget can be set to reach a set number of people per day or for the lifetime of the campaign (for example, one month leading up to the application deadline)

- **Activate Partner Organizations**
  - Share social media posts with MBIs and other partners, encouraging them to post and share with their networks
  - Develop web banners MBIs and other partners can post to their websites linking to the award information on the MBRF website
  - Purchase banner/e-Table of Contents ads in partner publications and relevant journals targeting mid career researchers

2. Announcing and Promoting the New PCP Resources

- **Leverage Social Networks**
  - Draft scheduled social media posts highlighting the importance of talking with older adults about cognitive health and driving back to specific resources for PCPs
  - Launch a Facebook ad campaign targeting primary care physicians and driving the to the PCP area of the site. Video clips of the cognitive assessment tool could be effective in driving traffic and attracting new site audiences

- **Activate Partner Networks**
  - Partner with the American Academy of Family Physicians to explore opportunities to post sponsored content on their site driving back to the new resources, guest blog on their website, advertise in their print and digital publications and more
  - Develop social media posts to share with MBIs and other partners, encouraging them to post and share with their networks
  - Develop web banners MBIs and other partners can post to their websites linking to the PCP are of the MBRF website

Education Statement

April 9, 2020

The McKnight Brain Research Foundation is the only private foundation dedicated exclusively to discovering the mysteries of the aging brain and helping people achieve a lifetime of cognitive health[1]. Elevating public awareness and understanding of cognitive aging and age-related memory loss is one of the Foundation's highest priorities. To meet this mission, we're working to fill the educational gaps and help primary care physicians recognize the signs of cognitive aging and age-related cognitive decline in order to help patients take action to maintain their brain health[1a/3a].

While one in eight people age 65 and older (13 percent) develops Alzheimer's disease, the remaining 87 percent are experiencing cognitive changes attributable to the normal aging process to varying degrees[2]. Unlike Alzheimer's disease and other neurodegenerative diseases, cognitive aging is not defined by a neurological or psychiatric disease or process[2a]. The brain changes associated with aging are part of a natural process that starts at birth and continues throughout the lifespan[2b]. While the brain ages just like the rest of the body, there is increasing evidence that cognition and brain health can be maintained with behavioral and lifestyle changes.

As the first point of contact to interact with patients, primary care physicians are best positioned to identify patients at-risk for or experiencing cognitive changes due to aging[3]. With the information and resources provided by the MBRF, they can and should be able to recommend or conduct screening during wellness visits and offer diet, exercise and lifestyle changes that have been proven to help maintain brain health[4/4a]. To learn more about these evidence-based recommendations and the importance of screening for cognitive changes, please visit the McKnight Brain Research Foundation website at: mcknightbrain.org[5/5a].

1. Intro to MBRF and our interest and role
    a. State our plan/intent to increase awareness and work to fill education needs/gaps for primary care
2. Note the large percentage that have CA/ML vs pathologies
    a. Note the difference between cognitive aging/memory loss and pathologies like Alzheimer's disease 87/13
    b. Define age-related memory loss
3. Note role that primary care has in being "front line" seeing these patients
    a. Note the need to increase awareness and education of primary care in this area
4. Cite the benefits and importance of screening during wellness visits by primary care
    a. Reinforce evidence-based recommendations like sleep, diet, activity etc
5. Link to the website resources, tools exist for assessment
    a. Recommend well validated tools for primary care

Content Outline for Primary Care Physicians Area of the McKnight Brain Website
June 4, 2020

Overview

The McKnight Brain Research Foundation seeks to develop a designated area of its website with tools and resources to help fill educational gaps and assist primary care physicians in identifying patients at-risk for or experiencing cognitive changes due to aging. Using the information and resources provided on the website, primary care physicians will also be able to recommend or conduct cognitive screening during wellness visits and offer tips on the diet, exercise and lifestyle changes that have been proven to help maintain brain health.

Suggested Content and Resources

What is Cognitive Aging?

- Cognitive Aging 101
- General Facts on Aging/Brain Health
- Benefits of Maintaining Brain Health
- Warning Signs and Behavior Changes

Prevention

- How to Maintain Brain Health
- Exercise for Brain Health
- Brain Healthy Diet Tips

Research Snapshots

- Highlight research from McKnight Trustees or MBI scientists with patient implications

Cognitive Assessment

- Importance of Cognitive Assessment
- Warning Signs
- Online Assessment Tool (3 options)
    - Link to outside trusted resources with descriptions of what each tool does and the differences
    - Create an online form – series of 10 questions PCPs can ask patients and a scoring tool based on the questions results
    - Create our own online assessment tool – PCPs and patients can walk through the McKnight Brain Assessment Tool together and question results will generate a doctor/patient recommendation upon completion

Patient Resources

- Fact Sheets and Resources to pass along to patients showing signs of cognitive decline and age-related memory loss:
    - How to Talk to Your Doctor
    - Treatment Options
    - Lifestyle Tips to Maintain Brain Health

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KEY MESSAGES FOR PRIMARY CARE PROVIDERS (PCPs)
MARCH 2023

Below are a set of recommended action steps primary care providers can proactively take during annual wellness visits or otherwise with adult patients of all ages to protect their patients' brain health.

Cognitive aging happens over a lifetime, and therefore patients should be encouraged at all ages, even as early as their 20s, 30s, and 40s, to pay attention to and mitigate risk factors to help them maintain brain health. The main source for the recommendations below is *Cognitive Aging – Progress in Understand and Opportunities for Action* (2015), a publication of the Institute of Medicine of the National Academies (found here).

1. Steps that Primary Care Providers can take to Promote Brain Health

- Use the Annual Wellness Visit as an opportunity to conduct preventive screenings including cognitive assessments. An overview of some of the more widely-used cognitive assessments can be found on the MBRF website. For additional information on how to code and bill for these assessments, visit Gerontological Society of America's KAER Toolkit, pgs. 3-8
- Educate patients about **health-promoting behaviors** which may reduce the risks of cognitive decline. Research-based recommendations include:
    - Staying physically active;
    - Reducing and managing cardiovascular disease risk factors including tight blood pressure control, weight reduction, cessation of smoking, and lowering cholesterol levels;
    - Encouraging family members to report any noticeable changes in the patient's cognitive abilities or memory;
    - Regularly reviewing any pertinent health conditions, medications, or supplements which may impact the patient's cognitive health;
    - Encouraging the patient to stay socially and intellectually engaged;
    - Discussing stress management and encouraging the patient to seek medical attention for any symptoms of depression, anxiety or any other mental health concerns;
    - Encourage eating a healthy and balanced diet that's low in fat and high in vegetables and fruit; and
    - Encourage getting the recommended amount of sleep while ruling out possible sleep disorders.

- Educate patients about **risk factors** which may increase the risk of cognitive decline. Research-based recommendations include:

    - Talk with patients about unhealthy behaviors that increase the risk of cognitive decline, such as cigarette smoking, excessive alcohol consumption, and a sedentary lifestyle;
    - Share evidence-based information regarding products that may be harmful or without benefit, including nutraceuticals and other interventions (PCPs may consult this evidenced-based web site on "Complementary Remedies" for older adults and Table 1 of this American Family Physician Article).

- Talk with your patients about the medicines they take and discuss possible side effects they may have on their memory, sleep and brain function (a helpful resource for this conversation is the Administration for Community Living's publication, "Brain Health: Medicine, Age, and Your Brain");

- Address perceptions, fears and common misunderstandings about aging and cognitive decline (for helpful tips on having this conversation, see Gerontological Society of America's KAER Toolkit, pages 11-12 and the National Institute on Aging's "Talking with your Older Patients");
- Intervene to minimize cognitive decline associated with medical conditions such as stroke, diabetes, head trauma, renal insufficiency, vision and hearing losses and cardiac disease;
- Upon admission to the hospital, screen for delirium risk factors and implement delirium-prevention strategies.

2. PCP Resources and Patient Handouts

Below are helpful handouts and resources that can be shared digitally, or in print, with patients:

- The MBRF's brochures explain the concepts of brain health and cognitive aging and include healthy lifestyle recommendations that benefit brain health.
  - "Keeping Your Brain Healthy" (digital and print, brochure)
  - "Cognitive Aging Explained" (digital and print, brochure, *in development*)
  - "Top 10 Tips for Healthy Aging" (digital and print, tips sheet)
- National Institute on Aging (NIA)
  - Cognitive Health and Older Adults (article)
  - What Do We Know about Healthy Aging? (article)
  - A variety of "Free Publications" produced by the NIA can be found here
- U.S. Department of Health and Human Services, Administration for Community Living (ACL)'s handouts review the basics of brain health:
  - "Talking About Brain Health And Aging - The Basics" (handout)
  - "Talking About Brain Health And Aging - The Basics" (PowerPoint Presentation for Providers and Educators)
  - "Brain Health: Medicine, Age, and Your Brain" (handout)
- American Heart Association's "Life's Essential 8™ Fact Sheet" (handout)

3. The Case for educating patients about their Brain Health

Overwhelmingly, Americans report wanting to learn how to "stay sharp," yet also report having little awareness about brain health research. PCPs can be the accessible, trusted, and familiar conduit of information and guidance on lifestyle habits and changes that patients can make to maintain and preserve their brain health.

Two-thirds of individuals report having little or no knowledge about brain health research (August 2022)

Commissioned by Research!America in partnership with the Dana Foundation, an August 2022 national survey captured Americans views on brain health and brain health research. Despite the widespread personal impact of brain health issues, 66% of respondents reported having little or no knowledge about brain health research. Of interest is that the same percentage of respondents, 66%, indicated strong curiosity to learn more. (Source)

"The 87%", The Journals of Gerontology, Series A, Vol 67, Issue 7, July 2012 - Molly V. Wagster, PhD, et al

- One in eight people 65 and older (13 percent) develops Alzheimer's disease.
- The remaining 87 percent are experiencing cognitive changes attributable to the normal aging process to varying degrees.

AARP 2016 Member Opinion Survey Results

- 84 percent of members surveyed (age 50 and older) were very concerned with staying mentally sharp.
- Staying mentally sharp (90 percent) and physically fit (87 percent) were the top two health/self-related interests among those surveyed.

KEY MESSAGES FOR CONSUMERS
MARCH 2023

The information below can be shared with individuals, family members, and caregivers to help advance their knowledge around cognitive aging and the steps they can take to preserve their brain health. Even small lifestyle changes can have significant benefits and may help older adults maintain their cognitive health. Research shows that a combination of these healthy behaviors may also reduce the risk of developing dementia. (Source)

Cognitive Aging Scientific Summary Statements

- Cognitive aging refers to the effect age has on cognition – including memory, thinking, learning, and problem solving – and is a normal part of getting older
- Cognitive aging affects individuals differently. Whereas some individuals experience cognitive changes in memory, for example, other may experience changes in other domains (e.g., proc speed, attention)
- The effects of cognitive aging may impact a person in subtle ways, such as not instantly finding the right word, or forgetting where you put your glasses.
- Cognitive training and physical activity interventions show promise for delaying or slowing age-related cognitive decline. (*Cognitive training is defined as a broad set of interventions, such as those aimed at enhancing reasoning, memory, and speed of processing.*)[1]
- The science of cognitive aging is still developing.

Key Messages for Consumers

1. What is Cognitive Aging?
As we age, our brains age too. Cognitive aging, like aging in general, is a natural process.

- Our brains age at different rates and in different ways.
  - Wisdom, expertise and vocabulary typically increase with age, while other abilities like processing speed, decision-making and some types of memory may decline.
  - The brain changes associated with aging are part of a natural process that takes place throughout our lives.
- Cognitive health is the ability to clearly think, solve problems, learn and remember. It's just one aspect of overall brain health and is an important part of protecting your ability to perform everyday tasks.

2. What is Brain Health?
Brain health is how well your brain functions across several areas, including:

- How well you think, learn and remember;
- How well you control your body movement, including balance;
- How well you interpret and respond to emotions; and

[1] National Academies of Sciences, E., et al., in *Preventing Cognitive Decline and Dementia: A Way Forward*, A. Downey, et al., Editors. 2017, National Academies Press (US)

- How well you make effective decisions.

3. What Can You Do to Maintain Brain Health?

- It's never too soon or too late to protect your brain health. Taking steps now, like staying physically active, getting enough sleep, and reducing and managing your risk for cardiovascular disease can help maintain your brain health as you age.

- Growing evidence shows there are various lifestyle behaviors that may help protect your brain health now and in the future. (Sources include National Institute on Aging and American Heart Association):
    1. **Exercise --** Break a sweat and engage in regular cardiovascular exercise that elevates the heart rate and increases blood flow to the brain and body.
    2. **Quitting Smoking –** Reduce your risk of cognitive decline to levels comparable with those who never smoked.
    3. **Keeping a Healthy Heart --** The risk factors for cardiovascular disease and stroke — obesity, high blood pressure, and diabetes — also have been shown to negatively impact cognitive health. Preventing and managing high blood pressure and cholesterol will help protect the heart and take care of the brain.
    4. **Eating a Healthy and Balanced Diet –** Following a diet that's low in fat and high in vegetables and fruit has also been linked to reducing the risk of cognitive decline. Although research on diet and cognitive function is limited, certain diets, like the Mediterranean and Mediterranean-DASH (Dietary Approaches to Stop Hypertension), may help maintain brain health.
    5. **Getting Enough Sleep –** Not getting enough sleep may result in problems with memory and thinking, yet a third of American adults report regularly getting less than the recommended 7-8 hours of sleep. Help protect your brain by getting better sleep.
    6. **Staying Socially Engaged –** Social and intellectual engagement is important for brain health. Pursuing interesting and meaningful social activities will help you keep connections with others. Try volunteering at a local church or animal shelter or just share the activities you enjoy with friends and family.
    7. **Learning and Welcoming Challenges –** Challenging and activating the mind by reading, doing puzzles, building furniture, or playing games are good ways to encourage strategic thinking. Taking an online class or learning a new language will also help keep your mind sharp.
    8. **Don't Forget Mental Health** -- Some studies also link depression with increased risk of cognitive decline. Managing stress and seeking medical attention for any symptoms of depression, anxiety or any other mental health concerns will help optimize your brain health.

3. Consumers' Concern with Cognitive Aging and Memory Loss/Prevalence and Desire to Learn More

Given the lack of data quantifying the number of people affected by cognitive aging and the associated cost, the statistics below can be used to help frame the issue in terms of prevalence and concern.

"The 87%", The Journals of Gerontology, Series A, Vol 67, Issue 7, July 2012 - Molly V. Wagster, PhD, et al

- One in eight people 65 and older (13 percent) develops Alzheimer's disease.
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AARP 2016 Member Opinion Survey Results

- 84 percent of members surveyed (age 50 and older) were very concerned with staying mentally sharp.
- Staying mentally sharp (90 percent) and physically fit (87 percent) were the top two health/self-related interests among those surveyed.

Research!America Public Survey results (August 2022)

- Despite the widespread personal impact of brain health issues, 66% of respondents reported having little or no knowledge about brain health research. Of interest is that the same percentage of respondents, 66%, indicated strong curiosity to learn more. (Source)

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McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss

Founded in 1999 by Evelyn F. McKnight, the specific goal of the McKnight Brain Research Foundation (MBRF) is to better understand and alleviate age-related cognitive decline and memory loss.

While it has been stated that one in eight people 65 and older has Alzheimer's Disease, cognitive changes due to the normal aging process will affect many of the remaining 87%, impacting abilities like processing speed and decision-making and contributing to some types of memory loss. The McKnight Brain Research Foundation champions research to better understand age-related cognitive decline and memory loss and educate the public on how to maintain cognition and brain health while aging successfully.

As the only private foundation focused exclusively on differentiating cognitive aging, age-related cognitive decline and memory loss from pathological disease states, (such as Alzheimer's disease and related dementias), the MBRF has established a national platform for outreach to the scientific community and the public. To accelerate the mission of the MBRF, the Foundation has previously partnered with other institutions to establish McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, the University of Miami, and the University of Florida.

The McKnight Brain Research Foundation and the McKnight Brain Institutes are leaders in cognitive aging research. Together, they are committed to sharing innovations in research and practical suggestions for maintaining brain health with the public, while supporting research leading to better understanding and alleviating age-related cognitive decline and memory loss.

OUR COMMITMENT TO RESEARCH

With direct contributions from the MBRF and strategic initiatives led by the MBRF through partnerships with the National Institute on Aging through the Foundation for the National Institutes of Health, and the four McKnight Brain Institutes, more than $180 million dollars have been provided in funding research specifically targeted towards cognitive aging, age-related cognitive decline and memory loss. By supporting three Cognitive Aging Summits and commissioning the National Academy of Medicine's study and report on Cognitive Aging (https://www.nap.edu/catalog/21693/cognitive-aging-progress-in-understanding-and-opportunities-for-action), the Foundation has made great progress leading to the understanding and alleviation of the effects of age-related cognitive decline and memory loss over the last two decades.

In fulfilling its mission of *"nurturing scientists dedicated to exploring and pursuing innovative research to advance the understanding and alleviation of age-related memory loss"*, the MBRF has partnered with the American Academy of Neurology through the American Brain Foundation to fund two cognitive aging clinical translational research scholarships per year for five years. The program is designed to support physicians or PhDs who are committed to a research program in cognitive aging and memory loss and have completed their training within five years of application. Each scholarship is a two-year award for a total of $150,000. In addition to the Scholarship program, the MBRF has previously funded individual block grant research support for inter-institutional collaborators between the four McKnight Brain Institutes.

The MBRF now proposes to extend its mission of supporting the next generation of world-class research scientists in the field of cognitive aging and memory loss by targeting outstanding mid-career scientists who have already demonstrated a firm commitment to cognitive aging research. This group of scientists is at a key milestone in their career trajectory having already proven themselves to be committed to research in cognitive aging and clearly demonstrated their potential to become leaders in their field. By providing research funding to these promising investigators as they continue to embark upon independent careers, the MBRF proposes to build a core group of outstanding research scientists across the United States with the potential to lead transformative research in the field of cognitive aging.

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PROPOSAL

The MBRF proposes to establish the ***McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss***

a. Length of Award: three years, renewal annually after satisfactory review

b. Amount of Award: $250,000 per year with match from the host institution

c. The Foundation commits to funding the program for a five-year initial trial period which would have supported 6 scientists at the conclusion of the five-year cycle

BUDGET

Year 1	Two Awards	$500,000
Year 2	Four Awards	$1,000,000
Year 3	Six Awards	$1,500,000
Year 4	Four Awards	$1,000,000
Year 5	Two Awards	$500,000
MBRF Commitment		$4,500,000

ELIGIBILITY

All applicants for the award program must have:

- completed research/clinical training i.e. formal post-doctoral research training post-PhD and/or physicians who have completed post-residency fellowship training.
- a proven track record of research accomplishments in cognitive aging as indicated by their publications in high-impact journals, awards, and other metrics of peer recognition.
- tenure-track faculty in an academic institution in the United States with evidence of long-term institutional support as indicated by commitment of resources including laboratory space, start-up research funds and personnel. Candidates not in a tenure-track position are also eligible and should also demonstrate similar evidence of long-term institutional support and not be in a time-limited appointment.

The proposed MBRF initiative would add substantial start-up support for a period of three years to help these investigators develop and/or expand an outstanding research program in cognitive aging and memory loss. Each year, one award will be made to support studies focusing on clinical translational research and another toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss. For example, this support could be deployed towards conducting a pilot clinical trial, developing proof-of concept interventions to ameliorate age associated cognitive impairment, gather preclinical data to accelerate testing of potential interventions, and further study the mechanistic basis of age-associated cognitive impairment with a view to identifying novel treatment targets. Scientists proposing to pursue basic research should clearly articulate the potential of their findings to be translated.

For Immediate Release:

Contact: John Chaich
john@afar.org

AFAR and the McKnight Brain Research Foundation launch new grant program in Cognitive Aging and Memory Loss

New program encourages outstanding mid-career scientists to lead transformative research in the field of cognitive aging.

NEW YORK and ORLANDO— The American Federation for Aging Research (AFAR) and the McKnight Brain Research Foundation (MBRF) are pleased to announce the launch of a new grant award program, **The McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss.**

The MBRF Innovator Awards in Cognitive Aging and Memory Loss are supported by a $4.5 million grant from the McKnight Brain Research Foundation and will support six investigators over a period of five years. Each year, MBRF and AFAR will provide up to two three-year awards of $250,000 annually. The total award amount of $750,000 over the three-year period will add substantial start-up support to help mid-career scientists develop and/or expand outstanding research programs in cognitive aging and memory loss.

The awards will be given in three grant cycles, in which each year, one award will be made to support studies focusing on clinical translational research and another award toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss.

“For most Americans, staying ‘mentally sharp’ as they age is a very high priority,” said Michael Dockery, MD, Chair of the McKnight Brain Research Foundation board of trustees. “Even those not affected by Alzheimer’s disease or other dementias will likely undergo cognitive changes due to the normal aging process. With the population of older adults growing rapidly in the United States and across the globe, it is critical that we support researchers dedicated to better understanding and alleviating the effects of age-related cognitive decline and memory loss.”

AFAR has long supported the careers of talented investigators and research on cognitive health. “By providing research funding, AFAR and MRBF are building a cadre of outstanding research scientists across the United States who have the potential to lead transformative research in the field of cognitive aging,” says Stephanie Lederman, EdM, Executive Director, AFAR.

With the new program, MBRF is extending its mission of supporting the next generation of world-class research scientists in the field of cognitive aging and memory loss by targeting outstanding mid-career scientists who have already demonstrated a firm commitment to cognitive aging research and shown the potential to become leaders in the field.

“Providing funding at the mid-career stage capitalizes on a unique opportunity to encourage leading scientists to continue embarking on independent careers that will lead to faster development of new ideas and approaches in cognitive aging research than is possible with traditional funding,” notes Lederman.

“We are excited to partner with AFAR and look forward to seeing the impact of the research bolstered through the new Innovator Awards in Cognitive Aging and Memory Loss,” Dockery added.

More information on the grant program and application can be found here: www.afar.org/grants/mcknight-award.

###

About AFAR
The American Federation for Aging Research (AFAR) is a national non-profit organization that supports and advances pioneering biomedical research that is revolutionizing how we live healthier and longer. For four decades, AFAR has served as the field's talent incubator, providing more than $184 million to more than 4,200 investigators at premier research institutions nationwide. A trusted leader and strategist, AFAR also works with public and private funders to steer high quality grant programs and interdisciplinary research networks. AFAR-funded researchers are finding that modifying basic cellular processes can delay—or even prevent—many chronic diseases, often at the same time. They are discovering that it is never too late—or too early—to improve health. This groundbreaking science is paving the way for innovative new therapies that promise to improve and extend our quality of life—at any age. Learn more at www.afar.org or follow AFARorg on Twitter and Facebook.

About the McKnight Brain Research Foundation
Founded in 1999, the McKnight Brain Research Foundation is the nation's only private foundation devoted exclusively to discovering the mysteries of the aging brain. By supporting research and investigation, we're working to better understand and alleviate the effects of age-related cognitive decline and memory loss. Learn more about the Foundation at: www.mcknightbrain.org.

2024 McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

The McKnight Brain Research Foundation (MBRF) and the American Federation for Aging Research (AFAR) will provide up to two 3-year awards of $750,000 (USD) each to advanced Assistant Professors and recently appointed Associate Professors (MDs and PhDs.) One award will be made to support studies focusing on clinical translational research and another award toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss.

The application deadline is August 12, 2024.

The Program

The major goal of the program is to identify emerging scientific leaders by building a cadre of outstanding research scientists across the United States to lead transformative research in the field of cognitive aging.

The program targets full-time independent investigators at the rank of Assistant Professor or Associate Professor (or equivalent) with established independent research programs who have already demonstrated a firm commitment to cognitive aging research. It will add substantial start-up support for a period of three years to help these investigators develop and/or expand an outstanding research program in cognitive aging and memory loss.

One award will be made to support innovative studies focusing on **clinical translational research** and another will support innovative studies of **basic biological mechanisms** underlying cognitive aging and age-related memory loss. It is expected that the proposed research will yield transformative discoveries and thus proposals are invited that are high risk/high gain in nature and that would be less suitable for conventional sources of funding. For example, this support could be deployed towards conducting a pilot clinical trial, developing proof-of concept interventions to ameliorate age associated cognitive impairment, gather preclinical data to accelerate testing of potential interventions, and further study the mechanistic basis of age-associated cognitive impairment in relevant experimental models with a view to identifying novel treatment targets. Scientists proposing to pursue basic research should clearly articulate the potential of their findings to be translated into clinically relevant strategies, and/or treatments. Research studies at the intersection of age-associated cognitive changes and disease-related cognitive impairment may be considered if a strong case can be made for their relevance to cognitive aging and age-related memory loss. However, research that is primarily focused on neurodegenerative diseases (e.g., Alzheimer's disease) will not be supported.

Two 3-year awards of $750,000 (USD) each will be made in 2024, of which a maximum of 10% may be used for indirect expenses or institutional overhead.

Eligibility

To be eligible, the applicant must:

- Have completed research training prior to the beginning of this award (October 1, 2024):
  o PhD candidates: no more than 7 years from the completion of formal post-doctoral research training post-PhD,
  o MD or combined degree candidates: no more than 12 years from the date when finished residency.
- Exceptions to the 7 and 12 year limits may be considered for certain life events (e.g. familial, personal commitments or other exceptional circumstances). An exception request can be submitted by emailing an NIH-style biosketch to AFAR at **grants@afar.org** at least one week prior to the deadline date.
- Be an independent investigator at the rank of Assistant Professor or Associate Professor (*promoted to the rank of Associate Professor* no earlier than October 1, 2021), who has received R01 funding (or equivalent funding such as an NIH DP5, R35 or NSF Research awards.)
- Be tenure-track faculty or equivalent in an academic or non-profit institution with evidence of long-term institutional support as indicated by commitment of resources including independent laboratory space, start-up research funds and personnel. Candidates not in a tenure-track position are also eligible and should demonstrate similar evidence of long-term institutional support and not be in a time-limited appointment.
- Have a proven track record of research accomplishments in cognitive aging as indicated by their publications in high-impact journals, awards, and other metrics of peer recognition.
- Provide evidence of institutional commitment as described in a **form completed by the Dean or CEO of the Institution** and a letter of commitment signed by the Department Chair.
- Be in full time employment at an academic or non-profit research institution in the United States.

The program **does not** provide support for:

- Senior faculty, i.e., at the rank of Associate Professor or higher who have held this position before October 1, 2021.
- Assistant Professors who have not yet received R01 or equivalent extramural independent funding.
- Investigators who are conducting research at a federal government or for-profit institution.
- See comment above about disease specific research.

Questions about eligibility and suitability of research project can be addressed to **grants@afar.org**.

Selection Criteria

Five criteria are used to determine the merit of an application:

- Qualifications of the applicant;
- Quality and promise of the proposed research and its relevance to cognitive aging/age-related memory loss;
- Novelty/impact of the proposed research and potential to have transformative clinical impact;
- Excellence of the research environment;
- The commitment by the institution to the applicant as described in the institutional commitment form and letter.

Application Procedures and Timeline

Please refer to the **application instructions**. Incomplete applications cannot be considered. All applications must be submitted via email to **afarapplication@afar.org**.

The applications will be reviewed by a committee whose recommendations will be presented to MBRF and AFAR for final funding decisions.

Please review **this link** which includes suggestions for submitting an LOI or application to AFAR. Click **here** for our Frequently Asked Questions page. If you are using animals in your research, please review **Principles of Animal Use for Gerontological Research** or this recent webinar recording from the Nathan Shock Centers of Excellence: **https://nathanshockcenters.org...**

MBRF and AFAR will not provide reviewer critiques to any applicants at any review level.

Timeline:
Application deadline: August 12, 2024

Anticipated Award Announcement: September 30, 2024

Award Start Date: October 1, 2024

Reporting Requirements

Investigators will be required to submit a brief **narrative report** annually on the progress of their research. Final narrative and financial reports are required within three months following the end date of the award.

Annual Meeting

Recipients of this award are expected to attend the AFAR Grantee Conference. The purpose of the meeting is to promote scientific and personal exchanges among recent AFAR grantees and experts in aging research. Grantees are also expected to attend the annual inter-institutional meeting of the MBRF.

Funder

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

Founded in 1999 by Evelyn McKnight, the Foundation's specific goal is to better understand and alleviate age-related cognitive decline and memory loss. Cognitive changes due to the normal aging process may affect up to 87 percent of people age 65 and older, impacting abilities like processing speed and decision-making and contributing to some types of memory loss. The **McKnight Brain Research Foundation** works to champion research to better understand age-related cognitive decline and memory loss and educate the public on the steps that can be taken to maintain cognitive and brain health and age successfully.

In its first 25 years, the Foundation established Evelyn F. McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, and the University of Miami, and the Evelyn F. and William L. McKnight Brain Institute at the University of Florida.

By partnering with the Foundation for the National Institutes of Health, and with the support of four Cognitive Aging Summits and the National Academy of Medicine Cognitive Aging Report, we have made great progress to better understand the effects of age-related cognitive decline and memory loss over the last two decades.

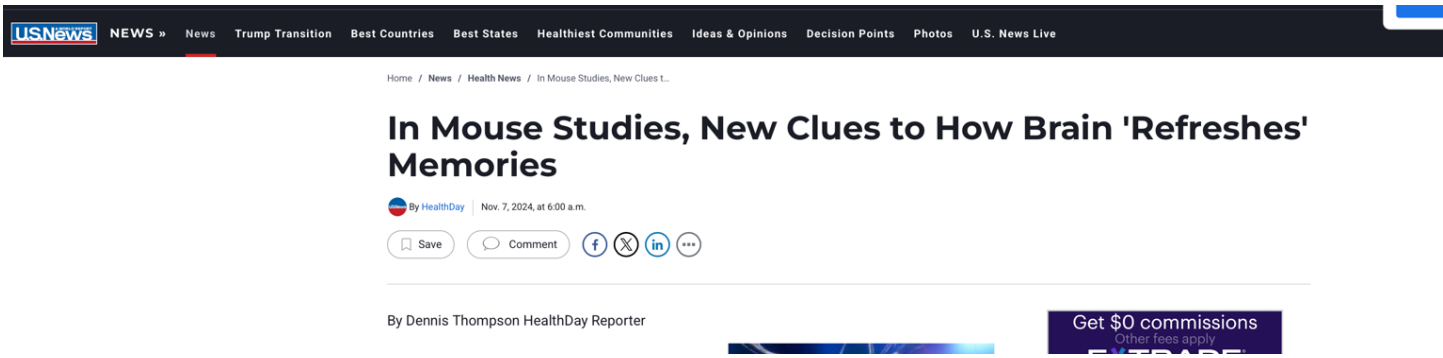
The McKnight Brain Research Foundation and the McKnight Brain Institutes are leaders in cognitive aging research. By providing research funding to promising investigators as they continue to embark upon independent careers, the MBRF proposes to build a core group of outstanding research scientists across the United States to lead transformative research in the field of cognitive aging.

Media Coverage

AFAR aims to track and share coverage of the Innovator Award recipients in popular media.

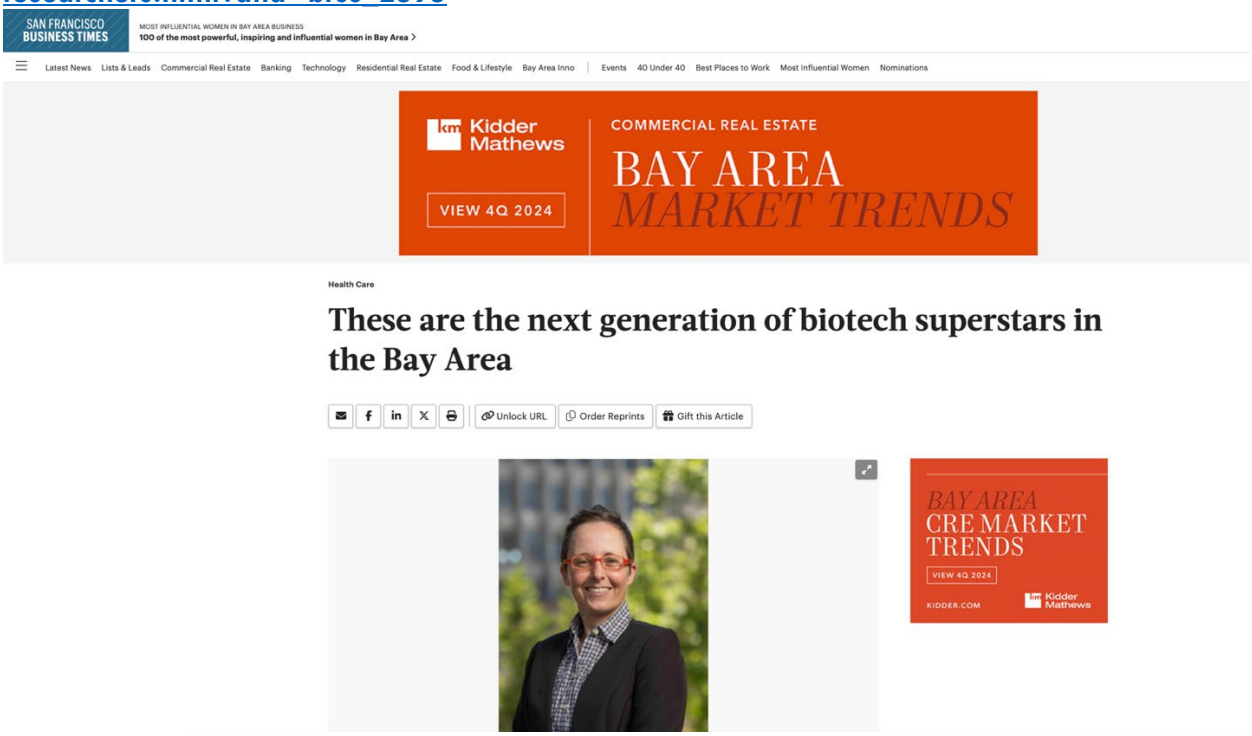
Please find below screen captures and links to reporting from institutions of several recipients in the first and second cohorts of the McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss recipients to date.

November 7, 2024, Denise Cai, PhD, in US News and World Reports
https://www.usnews.com/news/health-news/articles/2024-11-07/in-mouse-studies-new-clues-to-how-brain-refreshes-memories

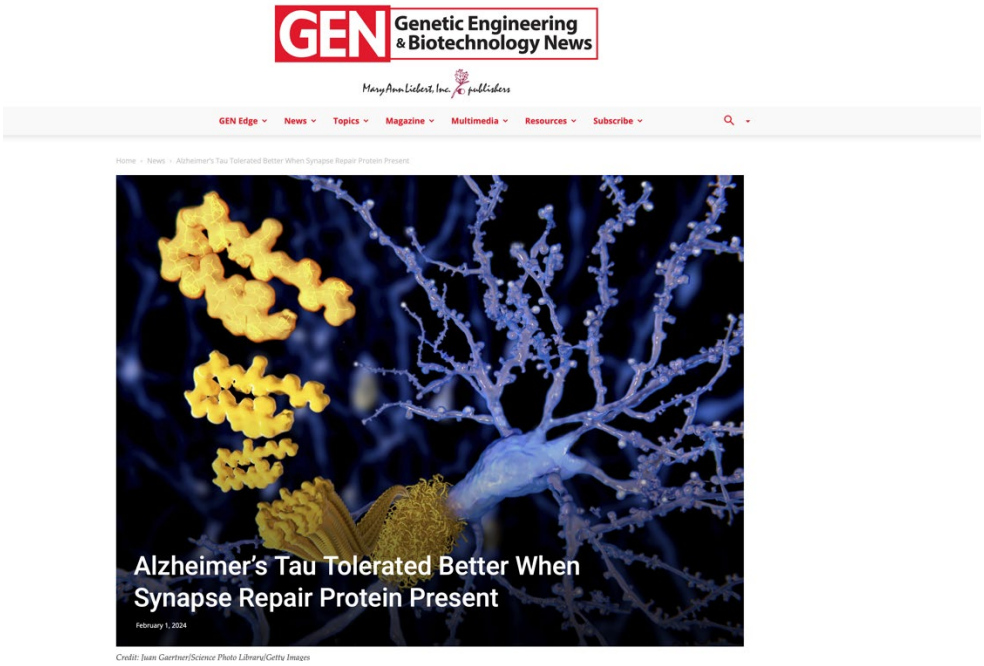


November 7, 2024, Denise Cai, PhD, in HealthDay
https://www.healthday.com/health-news/neurology/in-mouse-studies-new-clues-to-how-brain-refreshes-memories

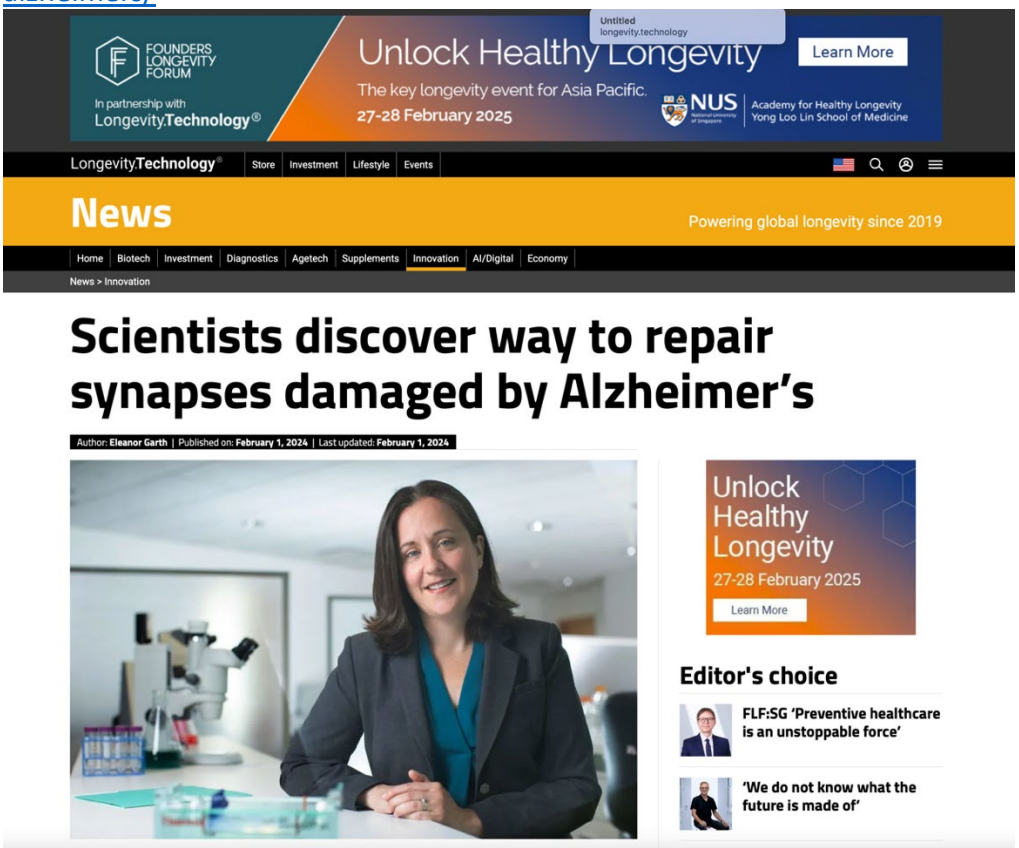
March 14, 2024, Tara Tracy, PhD, in San Francisco Business Times
https://www.bizjournals.com/sanfrancisco/news/2024/03/14/nex-gen-researchers.html?ana=brss_2896



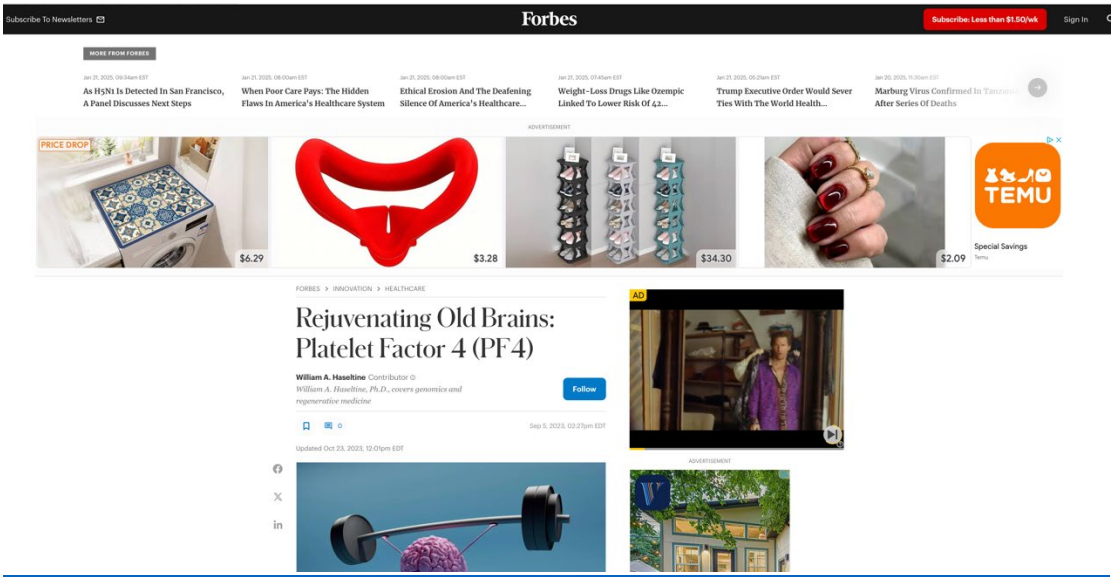
February 1, 2024, Tara Tracy, PhD, in Genetic and Biotechnology Engineering News
https://www.genengnews.com/topics/omics/alzheimers-tau-tolerated-better-when-synapse-repair-protein-present/



February 1, 2024, Tara Tracy, PhD, on Longevity Technology News
https://longevity.technology/news/scientists-discover-way-to-repair-synapses-damaged-by-alzheimers/



October 23, 2023, Saul Villeda, PhD, in Forbes
https://www.forbes.com/sites/williamhaseltine/2023/09/05/rejuvenating-old-brains-platelet-factor-4-pf4/

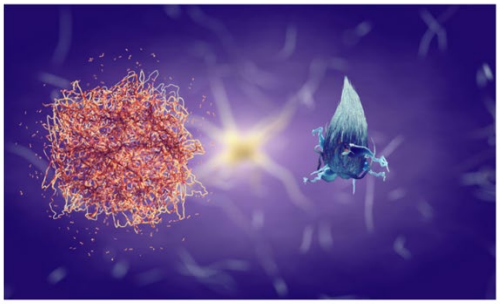


January 21, 2021, Tara Tracy, PhD, in Drug Target Review
https://www.drugtargetreview.com/news/100932/understanding-the-tau-tangles-in-neurodegeneration-could-aid-treatment-discovery/

NEWS

Understanding the tau tangles in neurodegeneration could aid treatment discovery

Representing a breakthrough in better understanding how tau proteins cause neurodegenerative disease, scientists have mapped the tau interactome.



By Mandy Parrett (Drug Target Review)

21 January 2022

No comments yet

SHARES

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The rise of organoids: a new era in drug discovery

Phage therapy: A step forward in the fight against antibiotic resistance

Academic Publications

AFAR aims to track and share coverage of the Innovator Award recipients' published research in academic publications.

Please find below screen captures and links to reporting from institutions of several recipients in the first and second cohorts of the McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss recipients to date.

November 6, 2024, Denise Cai, PhD, published in Nature
https://www.nature.com/articles/s41586-024-08168-4

nature

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nature > articles > article

Article | Open access | Published: 06 November 2024

Offline ensemble co-reactivation links memories across days

Yosif Zaki, Zachary T. Pennington, Denisse Morales-Rodriguez, Madeline E. Bacon, BumJin Ko, Taylor R. Francisco, Alexa R. LaBanca, Patlapa Sompolpong, Zhe Dong, Sophia Lamsifer, Hung-Tu Chen, Simón Carrillo Segura, Zoé Christenson Wick, Alcino J. Silva, Kanaka Rajan, Matthijs van der Meer, André Fenton, Tristan Shuman & Denise J. Cai

Nature **637**, 145–155 (2025) | Cite this article

20k Accesses | **328** Altmetric | Metrics

Abstract

Memories are encoded in neural ensembles during learning[1,2,3,4,5,6] and are stabilized by post-learning reactivation[7,8,9,10,11,12,13,14,15,16,17]. Integrating recent experiences into existing memories ensures that memories contain the most recently available information, but how the brain accomplishes this critical process remains unclear. Here we show that in mice, a strong aversive experience drives offline ensemble reactivation of not only the recent aversive memory but also a neutral memory formed 2 days before, linking fear of the recent aversive memory to the previous neutral memory. Fear specifically links retrospectively, but not prospectively, to neutral memories across days. Consistent with previous studies, we find that the recent aversive memory ensemble is reactivated during the offline period after learning. However, a strong aversive experience also increases co-reactivation of the aversive and neutral memory ensembles during the offline period. Ensemble co-reactivation occurs more during wake than during sleep. Finally, the expression of fear in the neutral context is associated with reactivation of the shared ensemble between the aversive and neutral memories. Collectively, these results demonstrate that offline ensemble co-reactivation is a

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Associated content

Nature Outlook

Sleep

Sections | Figures | References

February 1, 2024: Tara Tracy, PhD, published in The Journal of Clinical Investigation
https://www.jci.org/articles/view/169064

JCI The Journal of Clinical Investigation

KIBRA repairs synaptic plasticity and promotes resilience to tauopathy-related memory loss

Grant Kauwe,[1] Kristeen A. Pareja-Navarro,[1] Lei Yao,[1] Jackson H. Chen,[1] Ivy Wong,[1] Rowan Saloner,[2] Helen Cifuentes,[1] Alissa L. Nana,[2] Samah Shah,[1] Yaqiao Li,[3] David Le,[3] Salvatore Spina,[2] Lea T. Grinberg,[2,4] William W. Seeley,[2,4] Joel H. Kramer,[2] Todd C. Sacktor,[5] Birgit Schilling,[1] Li Gan,[6] Kaitlin B. Casaletto,[2] and Tara E. Tracy[1]

Authorship note: GK and KAPN contributed equally to this work.

Published February 1, 2024 - More info

View PDF

Abstract

Synaptic plasticity is obstructed by pathogenic tau in the brain, representing a key mechanism that underlies memory loss in Alzheimer's disease (AD) and related tauopathies. Here, we found that reduced levels of the memory-associated protein Kidney/BRAin (KIBRA) in the brain and increased KIBRA protein levels in cerebrospinal fluid are associated with cognitive impairment and pathological tau levels in disease. We next defined a mechanism for plasticity repair in vulnerable neurons using the C-terminus of the KIBRA protein (CT-KIBRA). We showed that CT-KIBRA restored plasticity and memory in transgenic mice expressing pathogenic human tau; however, CT-KIBRA did not alter tau levels or prevent tau-induced synapse loss. Instead, we found that CT-KIBRA stabilized the protein kinase Mζ (PKMζ) to maintain synaptic plasticity and memory despite tau-mediated pathogenesis. Thus, our results distinguished KIBRA both as a biomarker of synapse dysfunction and as the foundation for a synapse repair mechanism to reverse cognitive impairment in tauopathy.

November 21, 2023: Emilie Reas, PhD, Co-author publication in the Journal of Alzheimer's Disease
https://pubmed.ncbi.nlm.nih.gov/37955091/

Elevated Pure Tone Thresholds Are Associated with Altered Microstructure in Cortical Areas Related to Auditory Processing and Attentional Allocation

Linda K McEvoy [1] [2], Jaclyn Bergstrom [3], Donald J Hagler [4], David Wing [2], Emilie T Reas [5]

Affiliations + expand

PMID: 37955091 PMCID: PMC10793660 DOI: 10.3233/JAD-230767

Abstract

Background: Hearing loss is associated with cognitive decline and increased risk for Alzheimer's disease, but the basis of this association is not understood.

Objective: To determine whether hearing impairment is associated with advanced brain aging or altered microstructure in areas involved with auditory and cognitive processing.

Methods: 130 participants, (mean 76.4±7.3 years; 65% women) of the Rancho Bernardo Study of Healthy Aging had a screening audiogram in 2003-2005 and brain magnetic resonance imaging in 2014-2016. Hearing ability was defined as the average pure tone threshold (PTA) at 500, 1000, 2000, and 4000 Hz in the better-hearing ear. Brain-predicted age difference (Brain-pad) was calculated as the difference between brain-predicted age based on a validated structural imaging biomarker of brain age, and chronological age. Regional diffusion metrics in temporal and frontal cortex regions were obtained from diffusion-weighted MRIs. Linear regression analyses adjusted for age, gender, education, and health-related measures.

August 16, 2023: Saul Villeda, PhD, publication in Nature
https://www.nature.com/articles/s41467-023-39873-9

Article | Open access | Published: 16 August 2023

Platelet-derived exerkine CXCL4/platelet factor 4 rejuvenates hippocampal neurogenesis and restores cognitive function in aged mice

Odette Leiter, David Brici, Stephen J. Fletcher, Xuan Ling Hilary Yong, Jocelyn Widagdo, Nicholas Matigian, Adam B. Schroer, Gregor Bieri, Daniel G. Blackmore, Perry F. Bartlett, Victor Anggono, Saul A. Villeda & Tara L. Walker

Nature Communications **14**, Article number: 4375 (2023) | Cite this article

Abstract

The beneficial effects of physical activity on brain ageing are well recognised, with exerkines, factors that are secreted into the circulation in response to exercise, emerging as likely mediators of this response. However, the source and identity of these exerkines remain

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss Recipients

2024
Janine Kwapis, PhD, Assistant Professor and Paul Berg Early Career Professor in Biology, Pennsylvania State University
Sanaz Sedaghat, PhD, Assistant Professor, University of Minnesota

2023
Denise Cai, PhD, Associate Professor, Icahn School of Medicine at Mount Sinai
Christoph Thaiss, PhD, Associate Professor, Arc Institute

2022
Emilie Reas, PhD, Professor, University of California, San Diego
Tara Tracy, PhD, Assistant Professor, Buck Institute for Research on Aging

2021
Lindsay De Biase, PhD, Assistant Professor, University of California, Los Angeles
Saul Villeda, PhD, Assistant Professor, University of California, San Francisco

McKnight Brain Research Foundation
Clinical Translational Research Scholarship
in Cognitive Aging and Age-Related Memory Loss
and the McKnight Scholars and Mentors
April 2025

The McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss was established as a partnership with the American Brain Foundation in 2017. Ten McKnight Scholarships will be awarded for the period 2018 to 2022. The scholarships are funded by a $1.65 million grant from the McKnight Brain Research Foundation, through the American Brain Foundation (ABF) and the American Academy of Neurology (AAN).

This scholarship provides early career clinicians with $150,000 over two years in stipend and research-related costs. Applications for the award are open to young investigators interested in devoting significant research time in cognitive aging and age-related memory loss. The applications for the first two scholarships were submitted in 2017 and awards were made in spring of 2018.

The next application process will conclude on September 1, 2025. Review will take place in November of 2025 which will include three reviewers nominated by the McKnight Brain Research Foundation. Recipients will be notified in January 2026 and announcements made in early spring of 2026. It is hoped that the alumni scholars will present at the spring inter-institutional meeting of the MBIs in 2025.

McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss

Funded by the McKnight Brain Research Foundation through the American Brain Foundation and the American Academy of Neurology

Application Deadline: September 10, 2024

This award aims to support young investigators in clinical studies relevant to age-related cognitive decline and memory loss. The award also recognizes the importance of rigorous training in clinical research and encourages young investigators to seek opportunities to establish future careers in the area of human cognitive aging. **Please note: the focus should NOT be on a neurodegenerative dementia (e.g. Alzheimer's disease); however, proposals that focus on combined study of cognitive aging and neurodegenerative cognitive changes may be considered.**

The award will consist of a commitment of $65,000 per year for two years, plus a $10,000 per year stipend to support education and research-related costs for a total of $150,000. Supplementation of the award with other grants is permissible, but to be eligible to apply for this award, the other grant source(s) cannot exceed $75,000 annually.

The American Academy of Neurology is firmly committed to embracing the diversity among our members, applicants, and reviewers and affirms the importance of equity and inclusiveness within the AAN research program.

HOW TO APPLY

1. Visit AAN.com/view/ResearchProgram
2. Go to "2025 McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss"
3. Select "Apply now"

Please only submit one application - applicants are not allowed to submit applications for more than one award. Your application will also be considered for all relevant clinical research scholarship awards.

Visit the Frequently Asked Questions portion of the website for more information.

IMPORTANT DATES

September 10, 2024: Application deadline – Note that this is the deadline for all documents, including those from the mentor and chair. Applications will be declined if this information is not submitted by September 10.
January 2025: Notification of recipients
July 1, 2025: Funding begins

ELIGIBILITY

1. For the purpose of this scholarship, research is defined as patient-oriented research conducted with human participants, or translational research specifically designed to develop treatments or enhance identification of age-related cognitive decline and memory changes. These may include epidemiologic or behavioral studies, clinical trials, studies of disease mechanisms, the development of new technologies, and health outcomes research. Disease-related studies not directly involving humans are also encouraged if the primary goal is the development of therapies, diagnostic tests, or tools to mitigate age-related cognitive decline and memory loss.
2. Recipient is interested in an academic career in neurological research who has completed residency or a PhD no more than 5 years prior to the beginning of this award (July 1, 2025). If you have completed both residency and a PhD, your eligibility is based on when you completed residency. If you completed a fellowship of any kind after residency, your eligibility is still based on the date you finished residency. The applicant must hold a post-baccalaureate PhD degree or equivalent, or a doctoral-level clinical degree such as MD, DO, DVM, PharmD, DDS, DrPH, or PhD in nursing, public health or other clinical health science.
3. The proposed program of training and research must be performed entirely within an institution in the United States accredited by the relevant accrediting authority.
4. Research studies at the intersection of age-associated cognitive changes and disease-related cognitive impairment may be considered if a strong case can be made for their relevance to cognitive aging and age-related memory loss. However, research that is primarily focused on neurodegenerative diseases (e.g., Alzheimer's disease) will not be supported.

A successful application should include the following:

- Well-developed hypothesis: The hypothesis is testable and presented in clear language.
- Detailed statistical plan: Statistical methods are well-designed and detailed.
- Strong mentorship: There is clear demonstration of strong mentorship to support the project.
- Feasible primary outcomes: Each aim is feasible, focused, and logical.
- Innovation: Project concept is original, novel, and will advance the applicant's long-term career goals.
- Well-defined training plan: There is a clear and gap-based career development plan.

EVALUATION AND SELECTION

Applications are evaluated by reviewers based on the following criteria:

- Quality and originality of the research plan
- Applicant's ability and promise as a clinician-scientist based on prior record of achievement and career plan, and NIH Biosketch
- Quality and nature of the training to be provided and the mentor-specific, departmental, and institutional training environment
- Innovation of the research plan approach
- Project significance: the ability to advance the field of cognitive aging.

REQUIRED ATTACHMENTS FOR APPLICATION

1. PDF of Three-page Research Plan, including brief statements of aims, background, contemplated approaches to methodology and any supporting preliminary data/figures. References do not count toward the page limit. The research plan should be written by the applicant and should represent their original work. However, the applicant is expected and encouraged to develop this plan based on discussion with the proposed mentor.
2. PDF of Applicant's NIH Biosketch. See this link for the most recent NIH Biosketch template

Once the above information is fully completed and **submitted** by the applicant:

3. The **chair** will receive an email with a link asking them to check a box confirming that the applicant's clinical service responsibilities will be restricted to no more than 30 percent of the applicant's time and include a list of applicant's non-research related service. The chair will NOT be asked to submit a letter.
4. The **mentor** will receive an email with a link to submit a letter of reference detailing their support of and commitment to the applicant's proposed research and training plan. The letter should be 1,000 words or less and specifically indicate the mentor's role in the development and preparation of the applicant's research plan including:
    - How the proposed research fits into the mentor's research program
    - Expertise and experience in the area of research proposed and the nature of the mentor's proposed time commitment to the applicant's supervision and training
    - Mentor's prior experience in the supervision, training, and successful mentoring of clinician scientists
    - Potential for applicant's future research career and comparison of applicant to other trainees
    - Institution's commitment to 70 percent protected research time
5. The **mentor** will also be required to upload a NIH Biosketch.

ANNUAL AND FINAL PROGRESS REPORTS

An annual progress report is due in May of the first year. Renewal of the award in year two is contingent upon presentation of a satisfactory progress report. Additionally, a final research report and a final expenditure report are due within 60 days following the close of the grant term. The final expenditure report must be prepared by the institution's financial office.

CONTACT INFORMATION

Ilhan Mohamed, Research Grant Administrator
Phone: (612) 928-6028
Email: imohamed@aan.com

McKNIGHT BRAIN
RESEARCH FOUNDATION
Preserving memory, enhancing life

McKnight Brain Research Foundation Clinical Translational Research Scholarship Recipients

2025 (confidential until announced in April)
Giovanna Pilonieta, PhD, University of Alabama at Birmingham, Birmingham, Alabama
Deborah Rose, MD, Johns Hopkins University, Baltimore, Maryland

2024
Haopei Yang, PhD**,** Stanford University, Stanford, California

2023
Eva Klinman, MD, PhD, Washington University, St. Louis, MO
Sheena Baratono, MD, PhD, Beth Israel Deaconess Harvard Medical Center, Boston, MA

2022
Michael Kleinman, PhD, University of Miami Miller School of Medicine, Miami, FL
Sarah Szymkowicz, PhD, Vanderbilt University Medical Center, Nashville, TN

2021
Reem Waziry, MBBCh, MPH, PhD, Columbia University, New York, NY
Wai-Ying Wendy Yau, MD, Massachusetts General Hospital, Boston, MA

2020
Brian Baxter, PhD, Massachusetts General Hospital, Boston, MA
Sarah Getz, PhD, University of Miami Miller School of Medicine, Miami, FL

2019
Christian Camargo, MD, University of Miami Miller School of Medicine, Miami FL
Sanaz Sedaghat, PhD, Northwestern University, Chicago, IL

2018
Kimberly Albert, PhD, Vanderbilt University Medical Center, Nashville, TN
Brice McConnell, MD, PhD, University of Colorado Anschutz Medical Center, Aurora, CO

Communications

The McKnight Brain Research Foundation's

Brain Works Campaign Overview and Results to Date

Brain Works

Optimize Your Brain Span

Campaign Planning

- Conducted a landscape assessment to gather and glean information to help inform strategic communications program development.
- Audited and analyzed internal stakeholder feedback and external landscape on brain health and cognitive aging.
- Identified opportunities for strategic campaign/organization positioning, subject-matter white-space, influential voices, and like-minded existing campaigns.

Stakeholder Survey

Media and Digital Influencer Audit

Stakeholder Interviews

Review of Brain Health Campaigns

BRG

McKnight Brain Research Foundation's Unique Opportunity

The McKnight Brain Research Foundation has the opportunity to…

- ***Own the unique position as the nation's only private foundation dedicated to supporting research specifically on age-related cognitive decline and memory loss***
- ***Fill the void of public education about what normal brain aging is and what to expect***
- ***Clearly define what age-related cognitive decline and memory loss is separate from other issues related to cognitive aging***
- ***Reassure and guide younger to mid-life adults to better understand brain aging vs generating fear about the aging brain***
- ***Be a credible expert resource on brain aging for media and through social media***

Campaign Objectives

- **Create awareness and educate** the public about what normal brain aging is and what to expect
- **Reassure** and guide audiences on the topic of brain aging and work to mitigate fear
- **Reinforce** and elevate the McKnight Brain Research Foundation's brand as the nation’s only private foundation dedicated to supporting research specifically on age-related cognitive decline and memory loss
- **Encourage** HCPs to address and discuss brain aging with their patients

Strategic Approach

1. Reinforce MBRF's position as a leading research organization focused on cognitive aging by…. ***utilizing the credibility and voice of its board of experts and MBIs***

2. Reassure and guide adults by…. ***demonstrating what normal brain aging is and what to expect***

3. Act as a resource for healthcare providers by…equipping the HCP community ***with tools and information about cognitive aging they can share with their patients***

4. Be a convenor and collaborator with other leading aging and brain health organizations by…. ***creating a resource hub on the MBRF website to house resources for consumers and HCPs***

5. Reach younger audiences (35 – 50) who are paying attention to their health by….***engaging them with campaign messages and tools where they consume information***

6. Be deliberate and consistent with visibility to build share of voice by…***creating a surround sound to reach audiences multiple times through a variety of mediums***

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Campaign Components

CAPTURING CONTENT

- **Consumer Survey:** Public Knowledge / Perceptions on Brain Aging
- **HCP Viewpoint Research:** Experiences with Brain Aging and Patients
- **Utilize Findings:** Content creation and strategic guidance, including for the McKnightBrain.org website

BUILDING BRAIN AGING RESOURCE HUB

- **Online Destination:** Educate and engage audiences
- **Collaborate and Convene:** Create new resources and utilize select existing brain health insights and tools through link sharing
- **Tool Types:** Video vignettes, brain health quizzes and tests, scientific studies, downloadable content

TAPPING CHANNELS FOR VISIBILITY AND SHARE OF VOICE

- **Media Strategy:** Ongoing pitch effort, media tour, syndicated content, public service announcement and mass news distribution
- **Social Media:** Monthly content calendar of campaign posts, graphics, memes and more
- **Thought Leadership:** Conference speaking opportunities and byline articles
- **Power of Partnerships:** Information sharing and reaching niche audiences
- **Influencer voices:** Carry campaign messages on their own platforms

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Brain Works Three Year Campaign Roadmap

Year One – Build & Assess 2023-2024

- ✓ Survey and interview key stakeholders and Trustees
- ✓ Conduct landscape and media audit
- ✓ Analyze findings and develop campaign plan
- ✓ Develop creative concepts
- ✓ Build assets
- ✓ Launch campaign
- ✓ Initiate media relations and social promotion

Year Two – Create Momentum 2024-2025

- ✓ Evaluate program based on results
- ✓ Continue media outreach
- ✓ Build social engagement
- ✓ Develop strategic partnerships
- ✓ Engage HCPs
- ✓ Consider paid media opportunities – PSA or media partnership
- ✓ Build influencer and ambassador network

Year Three– Innovate & Expand 2024-2025

- ✓ Update campaign tactics based on metrics
- ✓ Continue media outreach and social engagement
- ✓ Amplify existing partnerships & create new opportunities
- ✓ Secure and promote media partnerships
- ✓ Enhance tools and content
- ✓ Deepen HCP engagement
- ✓ Consider new activations

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Measuring Success

DRIVE AWARENESS & EDUCATION	REASSURE & GUIDE AUDIENCES	REINFORCE & ELEVATE BRAND	ENCOURAGE HCPs to DISCUSS w/PATIENTS
• Media reach / impressions • Social media reach, engagement and website traffic • Digital influencer engagement • Thought leadership opportunities	• Resource downloads • Audience engagement with campaign tools • Message mentions around normal vs disease state • Partnership outcomes	• McKnight Brain Research Foundation's brand mentions in media • Expert voices quoted • Share of Voice • Speaking opportunities for MBRF Board and MBIs • Collaborative placements and activations	• HCP partner / sponsorship visibility and education • Thought leadership at HCP-focused conferences • Tools delivered through HCP community and environments to key audiences

Campaign Launch

The Brain Works campaign launched on Friday, March 22 with a satellite media tour to reach national television and radio audiences, along with social media activations and a national distribution of the Brain Works press release.

Campaign Launch Day (March 22)

- Satellite Media Tour featuring MBRF Vice Chair and Trustee Madhav Thambisetty
- Day of launch media outreach by BRG
- Press release distribution via national wire service
- Social/digital activation

Post-Launch Phase

April – June 30, 2024

BRG executed the following activities to continue a steady drumbeat of campaign visibility and media coverage following the initial launch.

- Ongoing Media Outreach
- Influencer Activation with Dr. Ben Rein (April 2024) and Additional Influencer Activations
- Audio and Video News Release Outreach (May 2024)
- Syndicated Article Activation (July 2024/ World Brain Day)
- Thought Leadership Opportunities
- Strategic Partnership Activations
- HCP Outreach
- Underserved Communities Targeted Outreach
- Reporting and Measurement

Year Two Campaign Activations

- ✓ Healthy Aging Month
- ✓ Ongoing Media Outreach
- ✓ Ongoing Digital Activations
- ✓ Building an Influencer and Ambassador Network
- ✓ Activating HCP and Community Partners

Overall Media Results

Campaign To Date Results

1.5B+
Impressions

4.1K+
Placements

50
Interviews

Year 2 Results

768M+
Impressions

95+
Placements

21
Interviews

Media Outreach Year 2 Goals

July 1, 2024– June 30, 2025

500M+
Impressions

2.5-5K+
Placements

30
Interviews

Digital Coverage by Numbers

Campaign To Date Results

562%
Follower Increase Across Platforms

24K
Webpage Views

Year 2 Results

441%
Follower Increase Across Platforms

25.5K+
Webpage Views

Digital Reach Goals Year 2

July 1, 2024– June 30, 2025

50%
Follower Increase Across Platforms

25-40K
Webpage Views

Brain Works

Optimize Your Brain Span

Upcoming Activity

Leveraging Key Timing Hooks

Media

- *National Outreach*
  - Nutrition Month (March)
  - Brain Awareness Week (March 9-15, 2025)
  - Sleep Awareness Week (March 10-16, 2025)
- *Syndicated Article*
- *Radio Media Tour*
  - Brain Awareness Week Hook

Influencers

- *Nutrition Expert*
  - *Tie into Nutrition Month*

Ongoing PSA Promotion

- *Digital promotion*
  - *Social*
  - *Web*

Brain Awareness Week

Sleep Awareness Week™

AAFP Partnership Overview

By leveraging AAFP channels and McKnight Brain Research Foundation resources and information, we can expand the reach of the Brain Works campaign resources and messages, empowering more patients to talk with their doctors about cognitive health and equipping physicians with additional tools to support their patients as they age.

Suggested Activations

- ✓ New articles to run on AAFP partner channels
- ✓ News story or blog post highlighting resources
- ✓ Online page featuring:
  - Articles
  - Infographic
  - Questions to ask your doctor
  - And more

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McKNIGHT BRAIN
RESEARCH FOUNDATION
Preserving memory, enhancing life

Thank You

BrainWorks
Optimize Your Brain Span

Brain Works Campaign Launch Message Framework
Approved March 1, 2024

The following message framework is designed to chart where key messages and supporting points ladder back to the objectives of the McKnight Brian Research Foundation's (MBRF) public education campaign, "Brain Works: *Optimize Your Brain Span*," on brain health and healthy cognitive aging. Below you will find primary messages with supporting messages and proof points.

These messages will be used in campaign materials including the news release, talking points and social media content. This is a living document that will be refined as we evolve the campaign and learn which messages resonate best with our audiences.

Campaign Objectives (Messages to ladder back to Objectives)

- Create awareness and educate the public about **what normal brain aging is and what to expect**
- **Reassure and guide audiences** on the topic of brain aging and work to mitigate fear
- **Reinforce and elevate MBRF's brand** as the only organization solely dedicated to funding research on age-related cognitive decline and memory loss
- **Encourage health care professionals** (HCPs) to address and discuss brain aging with their patients

CAMPAIGN MESSAGES

Message One: (Cognitive Aging)
Cognitive aging, or brain aging, is a natural part of the aging process, and may include some changes in the ability to think, learn and remember. Because many people may not realize these changes are normal with age, the McKnight Brain Research Foundation is committed to educating the public about brain aging, including the changes to expect and ways to maintain cognitive health with age.

Supporting Messages:

- While cognitive aging is part of the natural aging process and includes both positive and negative effects, most people don't know what to expect as they age. In fact, 1/3 of Americans who responded to a recent consumer survey by the MBRF said they feel uniformed when it comes to normal brain aging.

- The lack of understanding about cognitive aging translates into concern as shown by 87% of respondents to the MBRF survey stating they are concerned about age-related memory loss and decline in brain function as they grow older. This concern highlights the need to increase awareness and understanding for cognitive aging and what people can do to prioritize their brain health across the lifespan.

- Most people do not understand that age-related memory loss is usually associated with mild forgetfulness, which typically is part of normal aging and not necessarily a sign of a serious memory problem.

Message Two: (Campaign Introduction)

The McKnight Brain Research Foundation has created the "Brain Works: *Optimize Your Brain Span*" campaign to educate the public about what cognitive aging is and offer tips to help maintain optimum brain health with age. The campaign features information on cognitive aging, including an online hub of tools and resources from the McKnight Brain Research Foundation and other reputable expert organizations in cognitive health. The Foundation encourages the public to visit and learn more at McKnightBrain.org/BrainWorks.

Supporting Messages:

- While most people understand the need to pay attention to their brain health starting at an earlier age, they aren't sure what actions to take or where to look for accurate information. A recent survey by the McKnight Brain Research Foundation found the average age people think they should start focusing on brain health is 46.

- Despite recognizing the importance of focusing on brain health at an earlier age, the majority of survey respondents (57%) said they haven't discussed brain health or brain aging with their primary care provider. 62% said they haven't felt the need to and 21% believe they are too young to be concerned.

- Survey respondents also said that if they have sought out information on memory loss and cognitive decline, 42% looked for information on medical websites like WebMD and 39% turned to search engines like Google. The MBRF's Brain Works campaign will help people find comprehensive and accurate information on cognitive aging and brain health in one online destination.

- The McKnight Brain Research Foundation's Brain Works campaign was developed to help the public understand what cognitive aging is and encourage people to prioritize lifestyle choices to help optimize their brain health starting from an early age.

Message Three: (Brain Span and Actions)

While many people may focus on extending their lifespan with the goal of living as long as possible, they may overlook the importance of maintaining their health with age. Recognizing the importance of healthy aging to maximize quality of life, the MBRF is encouraging the public to "optimize their brain span" by taking important steps to help maintain a healthy brain across the lifespan.

Supporting Messages:

- There is growing evidence that various lifestyle modifications may help protect brain health now and in the future. These actions may include eating a healthy diet, participating in physical activity, and maintaining connections through social interaction.

- A recent MBRF survey showed that 74% of respondents recognize that the activities they participate in to care for their bodies will also help them care for their brain, while more than one-quarter miss the connection that taking better care of their body will also help take better care of their brain**.**

- There is a disconnect between what people believe can promote brain health and what they engage in. While 70% of MBRF survey respondents know exercise is helpful in maintaining brain health, only 57% do so, only 47% eat a healthier diet to protect their brain even though 69% are aware of the benefit. While 58% believe that social interaction is important for brain health, only half of respondents maintain social connections to benefit their brain health.

Message Four: (Concern/Fear)

The lack of understanding for cognitive aging - the age-related cognitive decline and memory loss that comes with the normal aging process – is a driving factor for fear and concern among the public. It's important to keep in mind that cognitive aging is not a disease, like Alzheimer's or dementia. With the Brain Works campaign, the MBRF is committed to helping mitigate fear by reassuring the public that brain aging is normal and providing practical lifestyle tips and information to help them reach and maintain optimal brain health.

Supporting Messages:

- The lack of knowledge around healthy brain aging could be causing the fear of developing a brain health related condition to out rank other health concerns. The recent MBRF survey found that 59% of respondents are most afraid of conditions that could affect their brain health as they age, while only 41% fear chronic conditions like cancer or diabetes.

- Misconceptions about age-related memory loss are causing concern about developing memory issues.66% of MBRF survey respondents asked about specific brain conditions worry about memory loss, 59% dementia, and only 44% are concerned about mental health.

Message Five: (About MBRF)

The McKnight Brain Research Foundation is the nation's only private foundation devoted exclusively to discovering the mysteries of the aging brain by supporting research to better understand and alleviate the effects of age-related cognitive decline and memory loss. The MBRF translates this research into resources and information that are accessible and engaging to the general public with the goal of helping people maintain a healthy brain throughout life.

Supporting Messages:

- Since its founding in 1999, the MBRF has funded more than $200 million in research specifically targeting age-related cognitive decline and memory loss through direct contributions and strategic initiatives in partnership with the four McKnight Brain Institutes and the National Institute on Aging through the Foundation for the National Institutes of Health.

- An established leader in the field of cognitive aging, the McKnight Brain Research Foundation established Evelyn F. McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, and the University of Miami and the Evelyn F. and William L. McKnight Brain Institute at the University of Florida.

- With its Board of Trustees made up of a diverse group with experience in neurology, geriatrics, research and primary care, the MBRF fosters cross-discipline, productive collaboration to advance cognitive aging research across its Trustees and the top brain health scientists studying and working at the McKnight Brain Institutes.

McKnight Brain Research Foundation
Brain Works: Optimize Your Brain Span Campaign
Media Coverage Report – March 22, 2024 - February 20, 2025

By The Numbers

1.5B+ Media Impressions **4.1K+ Placements**

Published Media Coverage

Podcast

- Living to 100 Club**:** Understanding Normal Aging and Brain Health: McKnight Brain RF, January 26, 2025
- Black Headline News Radio**:** Milton comes 11 days after Helene; hosts remember Amos; Dr. Brangman talks geriatric health and prevention live, October 8, 2024
- WomenOver70 Podcast**:** Sharon A. Brangman: The Phenomenon of Normal Cognitive Aging, October 3, 2024
- The Podcast by KevinMD*:* How to preserve your brain health, September 20, 2024
- Let's Talk Brain Health! Podcast*:* BrainWorks: Optimize Your Brain Span with Dr. Madhav Thambisetty, MD, PhD, August 14, 2024
- Aging Well Podcast**:** Episode 156: Revealing the Truth About Cognitive Aging w/ Dr. Roy Hamilton, June 9, 2024

National and International

- Fortune**:** The best science-backed strategies for a strong mind as you age, May 31, 2024
  Pick Up:
  - *AOL News*
  - *Yahoo! Finance*
  - *All Sides*
  - *Press Bee*
  - *Alpha Leaders*
  - *inkl*
  - *Ru24*
  - *MSN.com*
  - *Blogtop10*
  - *Yahoo! Canada*
  - *Cryptostudent*
  - *Vaping Underground*
  - *Zarko Palankov*
  - *Scott Barcomb*
  - *Qoshe.com*

- Authority Magazine: Brain Health*:* Dr Roy Hamilton Of The McKnight Brain Research Foundation On Lifestyle Habits Supporting Cognitive Well-Being, May 4, 2023

- Parade: The One Pre-Breakfast Habit Doctors Swear By for Dementia Prevention, January 20, 2025
  Pick Up:
  - *Review Canadian*

- Fortune: 5 ways to reduce your dementia risk as study estimates U.S. cases could double by 2060, January 16, 2025
  Pick Up:
  - *MSN.com*
  - *AOL.com*
  - *Inkl*
  - *Fortune Italia*

- Parade: TV and Video Games' Effects on Brain Health, January 10, 2025
  Pick Up:
  - *Yahoo! Life*
  - *News Break*

- Health: Study Reveals the Best (and Worst) Activities for Your Brain While You're Sitting Down, December 14, 2024
  Pick Up:
  - *MSN.com*
  - *Business and America*

- Black Health Matters: The Connection Between Brain Health & Holiday Loneliness, December 13, 2024

- Healthcasts**:** Understanding Brain Health in Aging Adults, December 13, 2024

- La Nacion: Incorporating these habits on a daily basis can benefit brain health, experts say, November 6, 2024

- TIME Magazine**:** 9 Things You Should Do for Your Brain Health Every Day, According to Neurologists, October 17, 2024
  Pick Up:
  - *Yahoo! Life*
  - *AOL.com*
  - *MSN.com*
  - *Our Community Now*
  - *Health Conscious*
  - *Easy Branches*
  - *Syfeed*
  - *iHeartEmirates*
  - *Head Topics*

- *Monitorul de Stiri*
- *Yahoo! Australia News*
- *Yahoo! Malaysia News*

- Oprah Daily**:** What Is Mild Cognitive Impairment?, October 3, 2024
  Pick Up:
  - *Yahoo! Life*
  - *MSN.com*
  - *AOL.com*

- AFRO**:** Experts say exercise and healthy life choices key in maintaining cognitive ability, September 28, 2024
  Pick Up:
  - *The San Bernadino American Newspaper*
  - *The Sacramento Observer*

- VeryWell Mind**:** This Is Your Brain on Exercise, September 24, 2024
  Pick Up:
  - *AOL.com*

- Parade: Want To Lower Your Dementia Risk? Don't Skip This Vaccine, September 15, 2024
  Pick Up:
  - *AOL.com*

- CBS Newspath – Eye on Health**:** Big change for mammogram screenings could save lives, September 13, 2024
  Pick Up:
  - *KYTX CBS19-TV*
  - *WMAZ-TV*
  - *WTOL-TV*
  - *WBNS-TV*
  - *WUSA-TV*
  - *WTSP-TV*
  - *WFMY-TV*
  - *WWL-TV*
  - *KHOU-TV*
  - *KREM-TV*
  - *KFMB-TV*
  - *KTHV-TV*

- VeryWell Health: Learning a New Language Is Hard, But Your Brain Will Thank You, August 16, 2024
  Pick Up:
  - *AOL.com*
  - *Yahoo! Lifestyle*

- Rolling Out: Sharon Brangman explains how to maintain cognitive health as we age, August 9, 2024

- Black Health Matters: Brain Aging: What's Normal & When Should We Worry?, July 24, 2024

- Well+Good: 11 Habits Neurologists Do Every Night for Better Brain Health—and How You Can Incorporate Them Too, July 12, 2024
  Pick Up:
  - *Internewscast Journal*

- Fortune**:** Is there a perfect age to be a leader?, July 6, 2024

- CBS Newspath – Eye On Health: Summer bump of COVID increasing across most of U.S. | Eye On Health, July 5, 2024
  Pick Up:
  - *CBS New York*
  - *WUSA-TV*
  - 23 other affiliates

- Fortune**:** What's happening inside an 80-year-old brain?, July 3, 2024
  Pick Up:
  - *AOL.com*
  - *Yahoo! Singapore Finance*
  - *Blogtop10*
  - *Don't Worry Buy*
  - *Alpha Leaders*
  - *Yahoo! Finance*
  - *Fortune China*
  - *Fortune Italia*

Local

- The Scott Solan Show: Podcast Interview, April 1, 2024

Campaign Launch Media Coverage

Satellite Media Tour Coverage
Total TV Placements: 12 broadcasts across 11 Stations

- WHAS- Louisville, KY
- KASY- Albuquerque (aired twice)
- KRQE- Albuquerque, NM
- WKEF- Dayton, OH
- WTVQ- Lexington, KY
- WHNT-Huntsville, AL
- KWGN/KDVR-Denver, CO

- WTVM-Columbus, GA
- KOKH-Oklahoma City, OK
- WHTM-Harrisburg, PA
- KXTV-Sacramento, CA

Total Radio Placements: 11 broadcasts

- KMA-AM Omaha, NE
- WGVS-FM Grand Rapids, MI
- WGVU-FM Grand Rapids, MI
- KXYL-AM Abilene, TX
- WYRQ-FM Minneapolis, MN
- KWAY-AM Cedar Rapids, IA
- WVNU-FM Cincinnati, OH
- WCUB-AM Green Bay, WI
- Valder Beebe Show
- WAMV-AM Roanoke, VA
- CRN Digital Talk Radio

Total Online Placements: 4 Placements

- Issues and Ideas with Chris DeBello
- KWGN/KDVR-Denver, CO – Online Article
- WTVM-Columbus, GA – Online Article
- KXTV-Sacramento, CA – Online Article

Video Wire Releases: 290 Placements

Total Newsbreak Placements - The Daily Flash & Daytime: 352 broadcasts across 259 stations

Total Audio News Release Placements: 1,468 broadcasts across 257 stations

Nationally Syndicated Article: 1,071 Placements

Cognitive Aging Explained

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

What is Cognitive Aging?

As we age, our brains age too. Cognitive aging is a natural process that can have both positive and negative effects and these effects vary widely from person to person.

Our brains age at different rates and in different ways. While wisdom, expertise and vocabulary increase with age, other abilities like processing speed, decision-making and some types of memory may decline with age.

Did You Know?

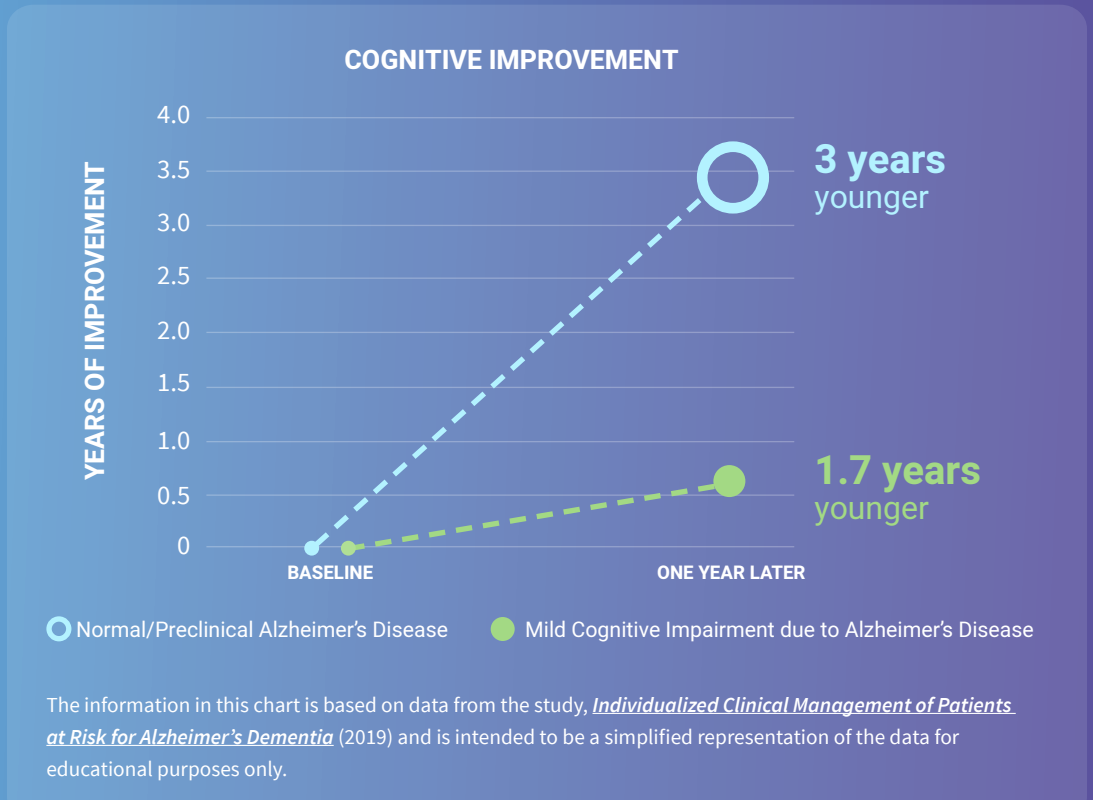
Cognitive health is the ability to clearly think, learn and remember. It's just one component of overall brain health and is an important component of performing everyday activities.

The research and information offered by the McKnight Brain Research Foundation are intended only for educational purposes and not to serve as medical or pharmaceutical advice.

Cognitive Aging Is Not a Disease

The brain changes associated with aging are part of a natural process that starts at birth and continues throughout the lifespan. Cognitive aging cannot be prevented, but there are steps you can take to optimize your brain and cognitive health.

Recent research found that adopting a series of lifestyle changes such as diet, exercise and challenging your brain by learning a new skill or starting a new hobby, helped people maintain and even improve their memory. The study examined the effects of individualized clinical management among people at risk for cognitive decline in a real-world clinic setting.



The information in this chart is based on data from the study, ***Individualized Clinical Management of Patients at Risk for Alzheimer's Dementia*** (2019) and is intended to be a simplified representation of the data for educational purposes only.

On average, after one year in the study, the cognitive function of a person with mild cognitive impairment (MCI) due to Alzheimer's disease looked like that of a person 1.7 years younger, and the cognitive function of someone with normal memory or preclinical Alzheimer's disease (i.e. exhibiting no evidence of cognitive impairment) looked like that of a person 3 years younger.

Optimizing Cognitive Health

A growing body of scientific research suggests the following factors promote cognitive health as you age:

Maintain your physical health.

- Get health screenings as recommended for your age.
- Talk with your doctor about the medicines you take and discuss the possible side effects they may have on your memory, sleep and brain function.
- Don't smoke or use other nicotine products.
- Get enough sleep – aiming for 7-8 hours every night.

Manage high blood pressure and other vascular conditions.

- Preventing or controlling high blood pressure may help your brain in addition to your heart.
- Observational studies have shown having high blood pressure in midlife – from your 40's to early 60's – increases the risk of cognitive decline later in life.

Keep your mind active.

- Staying intellectually engaged is one of the most powerful things you can do to maintain brain health.
- Reading books; playing games, like chess; solving crosswords; or learning a new skill, like a foreign language or photography can reduce your risk of developing cognitive impairment.

Eat healthy foods.

- Eating a healthy diet with a variety of fruits and vegetables, whole grains, lean meats, fish, poultry, and low-fat or nonfat dairy products can reduce the risk of many chronic diseases and promote brain health.

Engage in physical activity.

- Physical activity is beneficial for the brain and cognition.
- Aim for 30 minutes of physical activity every day.

Stay connected.

- Connecting with people through social activities and community programs may improve cognition and lower the risk of other health problems. It also helps improve mood and psychological functioning.

Manage stress and other mental health conditions.

- Stress is a natural part of life, but over time, chronic stress can negatively impact the brain, affect memory, and increase the risk for Alzheimer's and related dementia.
- Manage stress by getting help from a counselor or therapist, reaching out to friends and family for support, writing in a journal, and practicing relaxation techniques.

Memory & Aging

As you get older, it's normal to worry about your memory and thinking abilities. These changes are usually associated with mild forgetfulness – often a normal part of aging – and not a sign of a serious memory problem.

Know the Difference

Some normal signs of aging include:

- Making a bad decision once in a while
- Missing a monthly payment
- Losing track of time
- Not being able to find the right words
- Losing things around the house

Serious memory problems make it hard to do everyday things like driving and shopping. Signs may include:

- Asking the same questions repeatedly
- Getting lost in familiar places
- Inability to follow instructions or directions
- Becoming confused about time, people, and places

If you or a loved one is experiencing signs of a serious memory problem, talk with a doctor to determine whether the memory problems are normal and to find out what may be causing them.

Memory and other thinking problems have many possible causes, including depression, an infection, or medication side effects. Sometimes, the problem can be treated, and cognition improves. Other times, the problem is a brain disorder, such as Alzheimer's disease, which cannot be reversed.

Diagnosing

Talk to your doctor about any of the memory problems you're experiencing. Finding the cause of your memory problems is an important first step in determining the best course of action to address them.

ABOUT THE MCKNIGHT BRAIN RESEARCH FOUNDATION

The McKnight Brain Research Foundation is the only private foundation devoted exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health.

Our Strategic Pillars

Lead

First to establish a dedicated area of research specifically focused on age-related cognitive decline and memory loss

Inspire

Sharing information and research to help people maintain cognition and brain health for life

Partner

Forming partnerships and collaborations among scientists, institutions and organizations

Recognize & Reward

Offering scholarships and grants to attract bright young researchers and support current scientists

The McKnight Impact

$180,000,000

Funding over $180 million in research specifically targeting cognitive aging, age-related cognitive decline and memory loss through direct contributions and strategic initiatives in partnership with the four McKnight Brain Institutes and the National Institute on Aging (NIA) through the Foundation for the National Institutes of Health (FNIH)

240+

Researchers and five endowed Chairs supported across the four McKnight Brain Institutes

$15M

Awarded to FNIH - resulting in nearly 40 new grants over two cycles

10 scholars

Partnering with the **American Academy of Neurology** via the **American Brain Foundation** to fund ten cognitive aging research scholarships over five years

4 institutes

Established McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, the University of Miami and the University of Florida

3 summits

Hosted three successful Cognitive Aging Summits in partnership with the **NIA**, resulting in the Reserve and Resilience Program

1 report

Developed the **Cognitive Aging Report** in partnership with the **National Academy of Medicine** to promote cognitive health

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Keeping Your Brain Healthy

Brain Health Facts

It's a fact: your brain ages just like the rest of your body. It shrinks in size, slows down in speed, and becomes less adaptable to change as you age. While research on how to maintain brain health later in life continues at a rapid and expanding pace, we know there is growing hope and expectation that living longer, fuller cognitive lives is possible.

Brain health refers to how well your brain functions across several areas. Aspects of brain health include:

Cognitive Health

How well you think, learn and remember.

Motor Function

How well you make and control your movements, including balance.

Emotional Function

How well you interpret and respond to emotions – both pleasant and unpleasant.

Tactile Function

How well you feel and respond to sensations of touch, including pleasure, pain and temperature.

Tips to Maintaining Brain Health

Growing evidence shows that making behavioral and lifestyle changes can help you maintain cognition and brain health later in life.

Adopting a combination of healthy behaviors, which have also been shown to reduce cancer, diabetes and heart disease, will help you achieve maximum benefits for both your brain and body. And the good news is, **it's never too late** to adopt healthy habits.

Did You Know?

Brain health can be affected by age-related changes in the brain; injuries, such as stroke or traumatic brain injury; mood disorders, like depression, substance abuse or addiction; and diseases, like Alzheimer's disease.

Strategies to Protect Brain Health

Start adopting these 8 strategies today to protect your brain health now and in the future:

Exercise

Break a sweat and engage in regular cardiovascular exercise that elevates the heart rate and increases blood flow to the brain and body. Several studies have linked regular physical activity with a reduced risk of cognitive decline.

Quit Smoking

Evidence shows that smoking increases risk of cognitive decline. Quitting smoking can reduce that risk to levels comparable to those who have not smoked.

Get Enough Sleep

Not getting enough sleep may result in problems with memory and thinking, yet a third of American adults report regularly getting less than the recommended 7-8 hours of sleep. Help protect your brain by getting better sleep.

Stay Socially Engaged

Social and intellectual engagement is important to brain health. Pursuing interesting and meaningful social activities will help you keep connections with others. Try volunteering at a local church or animal shelter or just share the activities you enjoy with friends and family.

Keep a Healthy Heart

The risk factors for cardiovascular disease and stroke — obesity, high blood pressure and diabetes — also have been shown to negatively impact cognitive health. Preventing and managing high blood pressure and cholesterol will help protect the heart and take care of the brain.

Eat a Healthy and Balanced Diet

Following a diet that's low in fat and high in vegetables and fruit has also been linked to reducing the risk of cognitive decline. Although research on diet and cognitive function is limited, certain diets, like the Mediterranean and Mediterranean-DASH (Dietary Approaches to Stop Hypertension), may help maintain brain health.

Continue Learning and Welcome Challenges

Challenging and activating the mind by doing puzzles, building furniture or playing games are good ways to encourage strategic thinking. Taking an online class or learning a new language will also help keep your mind sharp.

Don't Forget Mental Health

Some studies also link depression with increased risk of cognitive decline. Managing stress and seeking medical attention for any symptoms of depression, anxiety or any other mental health concerns will help optimize your brain health.

Exercise for Brain Health

Did You Know?

Exercise is linked to stimulating the brain's ability to maintain and create network connections – which is linked to improvements in memory, learning, and spatial memory.

Physical activity is a valuable part of any overall body wellness plan and is associated with a lower risk of cognitive decline.

Many recent studies have linked regular physical activity with benefits for the brain. In fact, exercise has been linked to stimulating the brain's ability to maintain old network connections and make new ones that are vital to cognitive health, as well as increasing the size of a brain structure important to memory and learning and improving spatial memory.

Beneficial Exercises

Be sure to consult a doctor about your overall health before starting any new exercise program.

Aerobic Exercise

Aerobic exercise, such as brisk walking, is thought to be more beneficial to cognitive health than non-aerobic stretching and toning exercise. Research is ongoing, but aiming to move for about **30 minutes** on most days is shown to have many benefits.

Cardiovascular Exercise

Engage in cardiovascular exercise to elevate your heart rate, if you're able to do so safely. This will increase the blood flow to the brain and body, providing additional nourishment while reducing potential dementia risk factors like high blood pressure, diabetes and high cholesterol.

The More The Merrier

Incorporating other physical activities you may enjoy, like walking with a friend, taking a dance class, joining an exercise group or golfing may also be mentally or socially engaging. Activities can be as simple as bike riding, gardening or walking the dog.

Tips to a Brain Healthy Diet

Many foods, including blueberries, leafy greens, and curcumin (found in the spice turmeric), have been studied for their potential cognitive benefit. These foods were thought to have anti-inflammatory, antioxidant or other properties that might help protect the brain. So far, there is no evidence proving that eating or avoiding a specific food can prevent age-related cognitive decline.

While research on the relationship between diet and cognitive function is somewhat limited, it does point to the benefits of two specific diets that can reduce heart disease and may also be able to reduce the risk of cognitive decline: the DASH (Dietary Approaches to Stop Hypertension) diet and the Mediterranean diet.

The Dietary Approach to Stop Hypertension (DASH)

The DASH diet aims to reduce blood pressure and recommends:

Eating a diet that is low in saturated fat, total fat and cholesterol; and high in fruits, vegetables and low-fat dairy.

Consuming whole grain, poultry, fish and nuts.

Decreasing intake of fats, red meats, sweets, sugared beverages and sodium.

The Mediterranean Diet

The Mediterranean Diet incorporates different principles of healthy eating, typically found in the areas bordering the Mediterranean Sea and recommends:

Focusing on fruit, vegetables, nuts, and grains.

Replacing butter with healthy fats, like olive oil.

Limiting red meat.

Using herbs to flavor food instead of salt.

Eating fish and poultry at least twice a week.

ABOUT THE MCKNIGHT BRAIN RESEARCH FOUNDATION

The McKnight Brain Research Foundation is the only private foundation devoted exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health.

Our Strategic Pillars

Lead

First to establish a dedicated area of research specifically focused on age-related cognitive decline and memory loss

Inspire

Sharing information and research to help people maintain cognition and brain health for life

Partner

Forming partnerships and collaborations among scientists, institutions and organizations

Recognize & Reward

Offering scholarships and grants to attract bright young researchers and support current scientists

The McKnight Impact

$180,000,000

Funding over $180 million in research specifically targeting cognitive aging, age-related cognitive decline and memory loss through direct contributions and strategic initiatives in partnership with the four McKnight Brain Institutes and the National Institute on Aging (NIA) through the Foundation for the National Institutes of Health (FNIH)

240+

Researchers and five endowed Chairs supported across the four McKnight Brain Institutes

$15M

Awarded to FNIH - resulting in nearly 40 new grants over two cycles

10 scholars

Partnering with the **American Academy of Neurology** via the **American Brain Foundation** to fund ten cognitive aging research scholarships over five years

4 institutes

Established McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, the University of Miami and the University of Florida

3 summits

Hosted three successful Cognitive Aging Summits in partnership with the **NIA**, resulting in the Reserve and Resilience Program

1 report

Developed the **Cognitive Aging Report** in partnership with the **National Academy of Medicine** to promote cognitive health

McKNIGHT BRAIN
RESEARCH FOUNDATION

Preserving memory, enhancing life

www.mcknightbrain.org

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

25 YEARS

The McKnight Brain Research Foundation

Championing research to better understand and alleviate the effects of age-related cognitive decline and memory loss since 1999.

The McKnight Brain Research Foundation is the only private foundation devoted exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health.

Our Strategic Pillars

Lead
First to establish a dedicated area of research specifically focused on age-related cognitive decline and memory loss

Inspire
Sharing information and research to help people maintain cognition and brain health for life

Partner
Forming partnerships and collaborations among scientists, institutions and organizations

Recognize & Reward
Offering scholarships and grants to attract bright young researchers and support current scientists

The McKnight Impact

$200,000,000
Funding more than $200 million in research specifically targeting cognitive aging, age-related cognitive decline and memory loss through direct contributions and strategic initiatives in partnership with the four **McKnight Brain Institutes** and the **National Institute on Aging (NIA)** through the **Foundation for the National Institutes of Health (FNIH)**

400+
Researchers supported across the four McKnight Brain Institutes

$15M
Awarded to the Foundation for the National Institutes of Health resulting in 20 grant awards and four funding opportunities co-sponsored with the NIA

18 research awards
Partnering with the **American Academy of Neurology** via the American Brain Foundation and with the **American Federation for Aging Research** to fund talented cognitive aging investigators

4 institutes
Established **McKnight Brain Institutes** at the University of Alabama at Birmingham, the University of Arizona, the University of Miami and the University of Florida

4 summits
Hosted four successful Cognitive Aging Summits in partnership with the NIA through the FNIH, capturing national and international attention

1 report
Developed the **Cognitive Aging Report** in partnership with the **National Academy of Medicine** to promote cognitive health

McKNIGHT BRAIN RESEARCH FOUNDATION
Preserving memory, enhancing life
25 YEARS

In 2024, the McKnight Brain Research Foundation celebrated its 25th anniversary as the nation's only private foundation dedicated exclusively to discovering the mysteries of the aging brain. With the mission of better understanding and alleviating the effects of age-related cognitive decline and memory loss, the Foundation has funded more than $2 million in research to advance the field through direct contributions and strategic partnerships and initiatives.

Key Accomplishments

- Educating the public on cognitive aging and the steps to optimize brain health with the Brain Works campaign
- Supporting and bringing to light the discoveries and achievements of the four McKnight Brain Institutes
- Inspiring the next generation of scientists to pursue groundbreaking research on age-related memory loss and cognitive decline with the Innovator Awards and Clinical Translational Research Scholarships
- Collaborating with leading government agencies and organizations dedicated to aging and brain health to establish cognitive health as a key pillar of overall healthy aging

Learn more about our past, present and future direction in this anniversary video.

Watch Video

THE EVELYN F. McKNIGHT BRAIN INSTITUTE
UNIVERSITY OF ALABAMA AT BIRMINGHAM
Preserving memory, enhancing life

McKNIGHT BRAIN RESEARCH FOUNDATION
Preserving memory, enhancing life
Evelyn F. McKnight Brain Institute • University of Arizona

UNIVERSITY OF MIAMI MILLER SCHOOL OF MEDICINE
EVELYN F. McKNIGHT BRAIN INSTITUTE

UF Evelyn F. & William L. McKnight Brain Institute
UNIVERSITY of FLORIDA

The McKnight Brain Research Foundation and four McKnight Brain Institutes foster cross-discipline, productive collaboration among leading researchers to better understand and alleviate the effects of age-related cognitive decline and memory loss.

The scientific research conducted at the McKnight Brain Institutes examines the fundamental mechanisms that underlie the neurobiology of learning and memory and the influences contributing to successful aging. Findings and discoveries are applied clinically to help people maintain their cognitive health and manage the effects of age-related cognitive decline and memory loss.

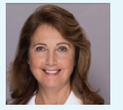
Evelyn F. McKnight Endowed Chairs

Recognizing Evelyn McKnight's generous support for ongoing brain research, the McKnight Brain Research Foundation established Endowed Chairs at each of the four McKnight Brain Institutes in her honor.

Dr. Ronald Lazar
Evelyn F. McKnight Endowed Chair in the Department of Neurology at the University of Alabama at Birmingham

Dr. Carol Barnes
Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at the University of Arizona

Dr. Ron Cohen and Dr. Tom Foster
Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory and Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging at the University of Florida



Dr. Tatjana Rundek
Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at the University of Miami

The University of Alabama at Birmingham

Established in 2004, the Evelyn F. McKnight Brain Institute at the University of Alabama at Birmingham (UAB) brings together scholars and researchers working in the forefront of basic, translational and clinical neuroscience, with the goal of addressing age-related memory and cognitive decline through: pre-clinical research to identify mechanisms as underlying targets for intervention; the conduct of translational studies that establish proof-of principle in human models; and the implementation of clinical trials that demonstrate safety and efficacy for mitigating memory and cognitive decline.

Evelyn F. McKnight Brain Institute Leadership

Director, Ronald M. Lazar, PhD, FAHA, FAAN

Director and Evelyn F. McKnight Endowed Chair, Dr. Ronald M. Lazar, is a graduate of New York University with a prize in Psychology and a PhD graduate in Psychology from Northeastern University. Since beginning his tenure with UAB in 2017, Dr. Lazar has worked to fulfill his vision of establishing new relationships with patient-oriented departments and clinical faculty and to build upon the already-existing strengths in basic and translational neuroscience at UAB.

Associate Director, Kristina Visscher, PhD

Associate Director, Dr. Kristina Visscher, received her PhD in Biological and Biomedical Sciences from Washington University in St. Louis and completed postdoctoral positions at Brandeis and Harvard Universities before joining the UAB faculty in 2009. Dr. Visscher is an Associate Professor in the UAB Department of Neurobiology and her research interests in cognitive neuroscience include investigating how the human brain can process the same environmental inputs in different ways at different time points.

Learn More About the Leadership Team on the UAB MBI Website →

Specialized Research on Cognitive Aging

Research at the UAB McKnight Brain Institute involves an interdisciplinary collaboration across departments and programs at the University of Alabama Birmingham and beyond, targeted at mitigating age-related cognitive decline in memory and cognitive function.

McKnight Brain Aging Registry (MBAR)

The McKnight Brain Aging Registry studies individuals who have been able to maintain high levels of cognition into older adulthood. Extensive data were collected from 200 adults over age 85 with excellent cognition. The collected data includes MRI images that depict the structure and function of the brain, extensive neuropsychiatric and behavioral test batteries, information about daily movements, and blood-based biomarkers. The data was collected as part of a significant investment in organizing and harmonizing data from across the four McKnight Brain Institutes.

Brain Health Advocacy Mission

The Brain Health Advocacy Mission (BHAM) is an initiative led by the UAB MBI to help people improve and maintain their brain health now and in the future. Enrolling patients age 18 and older, BHAM engages, empowers, and educates diverse populations on brain health with the goal of promoting healthy aging and memory loss prevention in Alabama and surrounding areas, by fostering meaningful connections in the community and primary care clinics.

Clinical and Population-based Research

Clinical and population-based research at the UAB MBI focuses on healthy aging throughout adulthood, as well as adults with age- related memory loss and cognitive decline, dementia, stroke and other cerebrovascular conditions. Areas of research include: cognitive resilience and recovery in aging; age-related cognitive function; and quality of life for the aging through research, education and clinical care.

Integrative Center for Aging Research

The Integrative Center for Aging Research serves as a hub for UAB investigators, providing support along the continuum of aging research from “Chromosomes to Communities.” The center also offers education, networking, and outreach opportunities for its multidisciplinary membership and local communities.

62
faculty members from 9 UAB academic schools and units

200+
peer reviewed publications annually in high impact journals

75+
percent of UAB MBI members have active extramural awards, including federal, foundations/ philanthropy, and industry

Learn more about the UAB MBI

The University of Arizona

Founded in 2006, the mission of the Evelyn F. McKnight Brain Institute at the University of Arizona is to discover the mysteries of the normally aging brain to achieve a lifetime of cognitive health.

Because of the inventive research of Dr. Carol Barnes and other affiliated faculty, along with the continual development of new technologies, the Evelyn F. McKnight Brain Institute is poised to contribute to southern Arizona as a center for high-level neuroscience, while also improving the understanding of brain and cognitive health for the entire world.

Evelyn F. McKnight Brain Institute Leadership

Director, Carol A. Barnes, PhD

Director, Dr. Carol A. Barnes is a Regents Professor in the Departments of Psychology, Neurology and Neuroscience, the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging, Director of the Evelyn F. McKnight Brain Institute and Director of the Division of Neural Systems, Memory and Aging at the University of Arizona, Tucson, Arizona. Dr. Barnes is past-president of the Society for Neuroscience, an elected Fellow of the American Association for the Advancement of Science, and an Elected Foreign Member of the Royal Norwegian Society of Sciences and Letters. She is also an elected fellow of the National Academy of Sciences.

Associate Director, Lee Ryan, PhD

Dr. Lee Ryan is a Professor in the Departments of Psychology and Neuroscience, Associate Director of the Evelyn F. McKnight Brain Institute, Director of the Cognition and Neuroimaging Laboratory, and Head of the Department of Psychology at the University of Arizona, Tucson, Arizona. Her work focuses on investigating the aging brain and how memory changes with age to identify ways to maintain a healthy brain through healthy lifestyle choices.

Learn More About the Leadership Team on the UA MBI Website →

Research on the Neurobiology of Cognitive Aging

The investigators at the Evelyn F. McKnight Brain Institute at the University of Arizona gain insights into brain function and cognition during aging using multiple animal models that include flies, rodents and nonhuman primates, as well as human participants. Institute investigators use cutting-edge and specialized behavioral assessments specifically created to be sensitive to those cognitive domains that change during normative aging, including tests for humans, as well as tests for the animal models of aging investigation.

Methods applied to understanding the mechanisms of brain aging that underly cognitive change with aging include state-of-the-art ensemble electrophysiological recording in behaving animals. The recordings can monitor changes in brain networks and cognitive decline in aged rodents and nonhuman primates and can be combined with live imaging methodologies.

Other large-scale molecular imaging technologies, like (the catFISH method) are also used allowing the examination of individual cells that participate in circuits critical for memory. Genetic, proteomic and epigenetic methods are also used by the EMBI researchers at the University of Arizona. In collaboration with our colleagues at the other McKnight Brain Institutes, these models are also used to understand changes in the molecular pathways that control cell function and are critical for brain plasticity mechanisms. The Evelyn F. McKnight Brain Institute in Tucson also shares and develops sophisticated methods for the collection of functional and structural MRI data in humans, and is a leader in developing machine learning and other advanced approaches for analyses of these data.

30+
affiliate faculty

200+
articles published annually on topics related to aging

$74M
in research funding

Learn more about the UA MBI

The University of Florida

The University of Florida Brain Institute, a world class $60 million building completed in 1998, was renamed the Evelyn F. and William L. McKnight Brain Institute of the University of Florida (UF MBI) in honor of a $15 million gift from the McKnight Brain Research Foundation in 2000.

Today, the UF MBI is one of the nation's foremost neuroscience and neuromedicine research centers. Its state-of-the-art, six-story building houses the laboratories of leading brain researchers and physician-scientists as well as the Advanced Magnetic Resonance Imaging and Spectroscopy Facility (AMRIS), a National MagLab facility.

More than a building, the UF MBI provides a robust scientific and intellectual environment that facilitates multidisciplinary understanding of nervous system function and dysfunction, spanning from the cellular level to translational research. The institute's 200-plus investigators seek to advance current knowledge to improve brain health across the lifespan and revolutionize the treatment of neural disorders.

Evelyn F. and William L. McKnight Brain Institute Leadership

Director, Jennifer L. Bizon, PhD

Dr. Jennifer Bizon is a professor and chair of the UF department of neuroscience. Within the UF College of Medicine, Dr. Bizon helped create a college-wide mentoring programs and serves as co-chair of the compensation committee and chair of the promotion and tenure committee. Dr. Bizon's research is broadly focused on understanding brain aging and its implications for cognitive function.

Deputy Director, Steven T. DeKosky, M.D.

Dr. Steven T. DeKosky is the Aerts-Cosper Professor of Alzheimer's Research in the UF department of neurology and associate director of the 1Florida Alzheimer's Disease Research Center. DeKosky is a recipient of the Henry Wisniewski Lifetime Achievement Award from the Alzheimer's Association.

Deputy Director, Jada Lewis, PhD

Dr. Jada Lewis is a professor of neuroscience and an investigator at UF's Center for Translational Research in Neurodegenerative Disease. She is a leader of the UF MBI's education and outreach efforts.

Deputy Director, Gordon Mitchell, PhD

Dr. Mitchell is the director of the UF Center for Breathing Research and Therapeutics (BREATHE) and an NIH-funded graduate and postdoctoral training program of the same name. He is a preeminence professor of neuroscience in the UF department of physical therapy.

Evelyn F. McKnight Endowed Chairs for Research

Tom Foster, PhD , Chair for Research on Cognitive Aging and Memory

Ron Cohen, PhD, Chair for Clinical Translational Research in Cognitive Aging and Memory

Learn More About the Leadership Team on the UF MBI Website →

THE MCKNIGHT BRAIN INSTITUTES

Specialized Research on Cognitive Aging

Center for Cognitive Aging and Memory Clinical Translational Research (CAM Center)

Co-directed by Sara Burke, PhD and Adam Woods, PhD, the CAM Center is a multidisciplinary center focused on brain aging and cognition, with leading researchers specializing in physiology, neurobiology of aging, neuroplasticity, pharmacology, clinical interests and computational, cellular and behavioral neuroscience. Research currently underway spans cellular, molecular and neural circuitry and includes designing and testing interventions to improve cognitive health in humans.

With strengths in both preclinical discovery-based research and clinical science, CAM Center researchers are dedicated to translating leading-edge brain aging discoveries into interventions to preserve cognitive function and improve the quality of life for older adults. The CAM Center is a fertile dynamic training ground for those interested in preclinical and translational research careers focused on optimizing cognitive aging.

200+
faculty members from more than 50 academic departments

50+
labs totaling 260,000 square feet of research space

2nd
ranked No. 2 in neuroscience and neuromedicine research for NIH funding among all public universities in the U.S.

Learn more about the UF MBI

Learn more about the CAM Center →

The University of Miami

Research at the Evelyn F. McKnight Brain Institute at the University of Miami is dedicated to advancing medical knowledge about memory loss and related neurological diseases.

UM MBI researchers are studying ways to improve the lives of people with Alzheimer's disease and other types of dementia, with a goal of developing new strategies to stop the disease process, minimize the impact on individuals, restore lost functions and eventually find the cause and cure for these devastating illnesses.

Evelyn F. McKnight Brain Institute Leadership

Director, Tatjana Rundek, M.D., PhD

Director and Evelyn F. McKnight Chair for Learning and Memory in Aging, Dr. Tatjana Rundek is a Professor of Neurology, Epidemiology and Public Health with tenure, Vice Chair of Clinical Research, and Director of the Clinical Translational Research Division in the Department of Neurology of the University of Miami, Miller School of Medicine. She holds a secondary faculty appointment at the Department of Neurology at Columbia University in New York.

Co-Associate Director, Bonnie Levin, PhD

Dr. Levin also serves as Division Chief for Neuropsychology and Cognitive Neuroscience and is a Schoninger/Goldberg Professor of Neurology. Her innovative neurocognitive research on the normative aging process focuses on the intersection of the physical, behavioral and sensory changes that occur over the life span.

Co-Associate Director, Ihtsham Ul Haq, M.D.

Dr. Ihtsham Haq also serves as Division Chief for Movement Disorders, the Cornfield/Hurowitz Chair in Movement Disorders and a Professor of Neurology. He conducts cutting-edge research to advance our understanding of the brain's functioning, combat age-related neurodegenerative disease and bridge the gap between neuroscience research and clinical applications.

Learn More About the Leadership Team on the UM MBI Website →

Cognitive Aging Research

The McKnight MRI Core and Neuropsychology Core Projects

The McKnight MRI Core and Neuropsychology Core Projects are collaborative core projects with other McKnight Brain Institutes involving ongoing research and collection of standardized brain MRIs and neuropsychological assessment data in patients with memory and cognitive loss.

Evelyn F. McKnight Brain Institute Cognitive Disorders Clinical and Biorepository Registry Collection

This comprehensive longitudinal database registry includes patients with age-related memory disorders and dementias. Participants are enrolled from the University of Miami Memory Disorders Clinic, a collaborative effort between Neurology and Psychiatry & Behavioral Sciences. The databank collects information on patient demographics, clinical assessments, medical history, genetic risk factors, imaging data and treatment modalities.

Identification of Biomarkers for Early Diagnosis of Cognitive Impairment in the Elderly

This ongoing study aims to identify new biomarkers that can be detected in participants who are at risk of developing dementia and/or who have cognitive impairment.

Evaluating Frailty as a Preventive Measure in Maintaining Quality of Life in Aging

This frailty research evaluates a clinical and community cohort of aging adults to determine their propensity towards being non-frail, pre-frail and frail, with the goal of early detection and prevention of frailty symptoms and clinical characteristics.

Analysis of Cognition in Patients with Memory Complaints

By analyzing patients with memory complaints, this research project examines questions related to the cognitive, psychological and biomedical variables associated with dementia and its subtypes, including demographics and risk factors that help identify predictive variables to improve the understanding of dementia and other memory disorders and their comorbidities.

1st

medical school in Florida, the Leonard M. Miller School of Medicine, founded in 1952

1962

Founding of the Department of Neurology, one of the oldest departments within the Miller School

100+

clinical and research faculty, with one of the largest neurology training programs

Learn more about the UM MBI

THE MCKNIGHT BRAIN RESEARCH FOUNDATION LEADERSHIP

Chair

Michael L. Dockery, MD
Charlotte, NC

Vice Chair

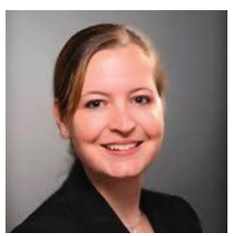
Madhav Thambisetty, MD, PhD
Ellicott City, MD

Chair Emeritus

J. Lee Dockery, MD
Gainesville, FL

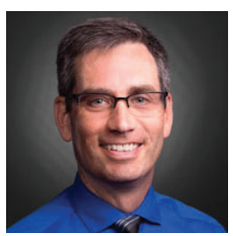
Corporate Trustee

Melanie A. Cianciotto
Orlando, FL



Trustee

Patricia A. Boyle, PhD
La Grange, IL



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Newport News, VA

Trustee

Sharon A. Brangman, MD
Syracuse, NY

Trustee

Allison Brashear, MD, MBA
Buffalo, NY

Trustee

Roy H. Hamilton, MD, MS
Philadelphia, PA

Trustee

Susan L. Pekarske, MD
Tucson, AZ

Evelyn F. McKnight, a nurse, established the Evelyn F. McKnight Brain Research Foundation® on May 26, 1999. Mrs. McKnight and her late husband, William L. McKnight, were interested in the effects of aging on memory. This interest inspired Mrs. McKnight to establish the Foundation as a legacy of support for brain research with the specific goal of better understanding and alleviating age-related cognitive decline and memory loss.

McKNIGHT BRAIN
RESEARCH FOUNDATION

Preserving memory, enhancing life

www.mcknightbrain.org

McKnight Brain Research Foundation (MBRF)

Charter of the Communications Working Group

An Advisory Group to the Board of Trustees

Purpose

The purpose of the Communications Working Group is to advise the McKnight Brain Research Foundation Board of Trustees on strategies to raise the level of public awareness about the importance and value to society of research in cognitive aging and age-related memory loss; to enhance public understanding of maintaining cognitive function and preserving memory; foster greater recognition of the history, achievements and current work of the McKnight Brain Research Foundation (MBRF); highlight the scientific research conducted within the network of McKnight Brain Institutes (MBIs); and share this information with the public in a relatable, engaging manner utilizing the McKnight network of experts.

The Communications Working Group will share expertise and ideas for elevating the McKnight Brain Research Foundation brand, will identify communication tools, resources, and audience segments, develop key messages, identify experts as possible spokespeople, identify media contacts, will suggest research of interest to the public, and will advise and recommend development of materials to share with MBRF and across the MBI network. The Communications Working Group will advise the MBRF Board of Trustees on the feasibility for national outreach including a public awareness campaign and will provide input into a communications plan to be reviewed and approved by the Board of Trustees.

Members

The Communications Working Group shall consist of 1 to 3 members from each McKnight Brain Institute. MBI Leadership shall nominate members who have expertise in one or more of these areas: communications, publications, marketing, website development, digital strategies, public relations, media relations, and/or other externally focused areas. Trustee Members will be appointed by the Chairman of the MBRF and, with the Chairman of the MBRF, these trustees will serve as ex officio members of the Communications Working Group. The Executive Director of the MBRF will serve as Chairman of the Communications Working Group.

Meetings

The Communications Working Group shall meet by phone at those times and places as determined by the membership of the group. The Communications Working Group may meet in person annually at the inter-institutional meeting of the McKnight Brain Institutes as determined by the Trustees of the McKnight Brain Research Foundation.

McKnight Brain Research Foundation and the McKnight Brain Institutes
Communications Working Group Members

July 2024

University of Alabama at Birmingham
Tasha Renee (Smith) Berry, PhD, MPH, Scientist II
Program Director, Evelyn F. McKnight Brain Institute
tasharsmith@uabmc.edu

University of Arizona
Vanessa Noonkester
Development Coordinator
Evelyn F. McKnight Brain Institute/Department of Psychology
Contact for Media, Donor Relations, Events, Marketing, Alumni, and Website
vnoonkester@nsma.arizona.edu

Peggy Nolty
Executive Assistant and Administrator
Evelyn F. McKnight Brain Institute/Department of Psychology
panotly@arizona.edu

University of Florida
Katie McIntyre
Administrative Specialist, Center for Cognitive Aging and Memory Clinical Translational Research
Evelyn F. and William L. McKnight Brain Institute
kathleenmcintyre@ufl.edu

Todd Taylor
Assistant Director of Communications
Evelyn F. and William L. McKnight Brain Institute
Tmtaylor4@ufl.edu

University of Miami
Christian J. Camargo, MD
Fellow, Division of Cognitive Neurology
Instructor, Department of Neurology
University of Miami Miller School of Medicine
ccamargo@med.miami.edu

Susan Fox-Rosellini, MBA
Executive Director of Advancement
Department of Neurology
University of Miami Miller School of Medicine
sfoxrose@med.miami.edu

McKnight Brain Research Foundation Trustees

Patricia Boyle, PhD
Trustee, Communications Committee Chair
paboyle@gmail.com

Lee Dockery, MD
Chair Emeritus
Jld007@cox.net

McKnight Brain Research Foundation Staff

Valerie Patmintra
Senior Communications Advisor
vpatmintra@mcknightbrain.org

Amy Porter
Interim Executive Director
aporter@mcknightbrf.org

McKnight Brain Research Foundation Senior Communications Advisor

Duties and Responsibilities

1. MBRF Communications Tools and Materials

- Maintain the MBRF logo and branding across all materials
- Develop new materials as needed, including brochures, fact sheets, FAQs, etc.
- Draft press releases and news announcements

2. MBRF Website and Social Media

- Draft and post new content to maintain the MBRF website
- Interview experts and draft posts for the monthly Ask the Experts blog series
- Develop themes and draft content on a monthly basis to make 3-4 social media posts each week.
- Plan and implement quarterly social media outreach campaigns

3. MBRF Media Outreach and Tracking

- Work with the MBIs to identify research stories and experts for potential media outreach
- Track media and social media metrics and reach throughout the year and provide quarterly updates to the Trustees

4. Communications Working Group

- Schedule and staff bi-monthly meetings with members of the Communications Working Group to engage in ongoing activities, including:
    - Sharing news announcements and research activities
    - Reviewing, vetting and approving MBI communications materials
    - Providing input on upcoming studies with relevant consumer/medical angles
    - Identifying young researchers and studies of note to highlight on the MBRF website and social media channels

Valerie Patmintra
Senior Advisor of Communications
McKnight Brain Research Foundation (MBRF)

Valerie Patmintra is a communications executive with more than 20 years experience developing and implementing successful marketing and communications programs for nonprofit organizations and Fortune 500 companies. Valerie serves as the Senior Advisor of Communications, to the MBRF. In this role, she provides ongoing communications support, including message development and implementation, content development and maintenance of mcknightbrain.org and organizational materials. She also provides social media strategy and content development, and media relations support.

Before beginning her work with the MBRF, Valerie served as the Director of Communications for the National Osteoporosis Foundation. In this position, Valerie developed and implemented the organization's annual marketing communications strategy to build and strengthen its role and reputation as the leading voice on osteoporosis. By building and maintaining national media relationships and serving as the organization's principal point of contact for media, she secured more than 400 million media impressions for the organization on average annually. She also implemented the organization's *Generations of Strength* awareness campaign and managed the public relations agency of record to secure more than 100 million media impressions for three-month campaign.

Valerie also served as the communications director for NOF's partner agency, the National Bone Health Alliance, and implemented the organization's first national awareness campaign, which resulted in more than 200 million media impressions with placements in top tier media outlets, including *Wall Street Journal*, *Associated Press* and *USA Today*.

Prior to joining NOF, Valerie served as a Senior Account Director for BRG Communications and led teams to develop award-winning national awareness campaigns for corporate and nonprofit clients, including the Home Safety Council, National Center for Healthy Housing, Medtronic and the American Osteopathic Association. She managed proactive and reactive media relations, resulting in feature segments and stories with top-tier media outlets, including The Today Show, *Good Housekeeping,* and *USA Today.* Valerie also developed and implemented the public relations and organizational communications strategy for the Home Safety Council's Silver Anvil award-winning Home Safety Month campaign that resulted in 200 million media impressions on average annually.

Valerie also served as a senior consultant with Booz Allen Hamilton and worked on teams supporting Kodak, SAP, and the Consumer Electronics Association while working in account management positions with Burson Marsteller and Weber Shandwick Worldwide. She holds a Bachelor of Science degree in Public Relations from the University of Florida and was a member of the Golden Key National Honor Society.

MBRF Gift Agreements
with the
McKnight Brain Institutes

Gift Agreements McKnight Brain Institutes (MBIs)

6. Evelyn F. McKnight Brain Institutes

A. University of Alabama at Birmingham (UAB)

1. Gift Agreements:

   a. May 1, 2004—Gift Agreement provided for a gift of $5 million from the MBRF to be matched by the UAB over a five-year period of time. The Purpose of the gift was to support research of the brain in the fundamental mechanisms of the aging brain that underlie the neurobiology of memory with clinical relevance to the problems of cognitive decline and age-related memory loss.

   The agreement also:

   - Established the Evelyn F. McKnight Brain Institute.
   - Established an endowed professorship for learning and memory in aging valued at $500,000.
   - Michael J. Friedlander, Ph.D., Chair of the Department of Neurobiology would occupy the endowed chair.

   b. October 19, 2005—Gift Agreement amended as follows:

   - The MBRF agreed to contribute an additional $1 million to convert the Endowed Professorship to the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $1.5 million.
   - The UAB agreed to match the additional $1 million contribution.
   - The amendment to the gift agreement specified the locations of the Evelyn F. McKnight Brain Institute would be the 9th, 10th and 11th floors of the newly constructed Shelby building.

   c. August 3, 2009—Gift Agreement amended as follows:

   - The amendment created a permanent $10 million Endowment.
   - MBRF and UAB **each** funded $5 million. ($1 million per year for five years).
   - The MBRF and the UAB would each contribute $500,000 per year for two years in addition to the endowment funds for operational costs.

2. Directors and Endowed Chairs: Chair Value: $1.5 million
   a. Director and Chair: David J. Sweatt, Ph.D.—2006-July 2016
   b. Interim Director: Dr. David Standaert, M.D. Ph.D.—July 1-May 31, 2017
   c. Director and Chair: Ronald M. Lazar, Ph.D.—June 1, 2017—present
   d. Associate Director: Eric Roberson, M.D., Ph.D. October 1, 2015 —December 31, 2022
   e. Associate Director: Kristina Visscher, PhD—January 1, 2023--Present
   f. Chair, Advisory Committee for MBI at UAB—Dr. David Standaert, June 1, 2017--Present

B. University of Arizona (UA)

1. Gift Agreements:

   a. October 17, 2006—Gift Agreement provided for a gift of $5 million from the MBRF matched by the UA over a five-year period of time. The purpose for the gift was for the overall support of the research of the brain intended for clinical application to accomplish alleviation of age-related memory loss.

   The agreement also:

   - Established the Evelyn F. McKnight Brain Institute.
   - Established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $1 million.

1.b. University of Arizona – Gift Agreements, Continued

- Named Carol A. Barnes, Ph.D., as the occupant of the endowed chair.

b. July 10, 2008—Gift Agreement amended as follows:

- The MBRF agreed to contribute an additional $300,000 to recruit a replacement for a departing research scientist critical to Dr. Barnes' research.

c. May 1, 2014—Gift Agreement amended as follows:

- Create a permanent $10 million Endowment.
- MBRF and UA each fund $1 million per year for five years.
- The MBRF and the UA would each contribute $200,000 per year for three years in addition to the endowment funds for operational costs.
- Both parties agreed that, if in any given year the match could not be made, funds in the amount equal to the amount which would be due for distribution on the value of the endowment at that time would be contributed by the defaulting party and will be cumulative until the obligation is met.

2. Directors and Endowed Chairs: Chair Value: $1.0 million

a Director and Chair: Carol A. Barnes, Ph.D.—2006—present

b. Associate Director: Lee Ryan, Ph.D.—2014—present

C. University of Florida (UF)

1. Gift Agreements

a. April 28, 2000-- Gift Agreement provided for a gift of $15 million from the MBRF matched by the state of Florida over a five-year period of time through a matching program approved by the state legislature to create a permanent endowment.

The agreement also:

- Established the Evelyn F. and William L. McKnight Brain Institute (MBI) of the University of Florida.
- Established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $4 million, ($2 million from the MBRF and $2 million from match).
- Established a $26 million McKnight Research Grant Fund ($13 million from the MBRF and $13 million match).
- The University agreed to fund the distribution of income for the McKnight Research Grant Fund as if the full match had been met, with decreasing commitments at the same rate as the increase in the level of match.

b. October 20, 2009-- Gift Agreement amended as follows:

- Established a Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP) within the Institute on Aging at the UF.
- Divided the $3.2 million investment income from the McKnight Research Grant Fund and transferred one-half ($1.2 million) to the newly established Cognitive Aging and Memory Research Fund for support of the CAM-CTRP.
- It was agreed one-half of the investment income would be equally divided between the CAM-CTRP and the MBI to support research in cognitive aging and age-related memory loss.
- The UF agreed to a national search for a qualified clinical research scientist as a program director.
- Marco Pahor, M.D., Director of the Institute on Aging, would act as interim program director as well as the scientific director until the program director was recruited.

1. b. University of Florida – Gift Agreements, Continued

- July 1, 2010—Jennifer L. Bizon, Ph.D., was recruited as Associate Professor in the Department of Neuroscience and joined Thomas C. Foster, Ph.D., as a faculty member in the Age-Related Memory Loss Research Program in the MBI.
- October 3, 2011--The McKnight Research Grant Fund account was closed and the McKnight the endowment account was continued as the McKnight Cognitive Aging and Memory Research Fund.
- July 1, 2012—Ronald A. Cohen, Ph.D., a cognitive neuropsychologist, was recruited as the director of the CAM-CTRP.
- July 1, 2013—Adam J. Woods, Ph.D., was recruited as assistant professor in the CAM-CTRP.
- October 1, 2013—Sara Burke, Ph.D., and Andrew Maurer, Ph.D., were recruited to join the Age-Related Memory Loss research faculty in the MBI.

c. July 1, 2015-- Gift Agreement amended as follows:

- Established the Evelyn F. McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging valued at $4 million.
- Funded the chair by taking $3 million from growth in the principle from the McKnight Cognitive Aging and Research Grant fund and $1million from the growth in the principal of Evelyn F. McKnight Endowed Chair Fund for Brain Research in Memory Loss.
- Dr. Ron Cohen was named the occupant of the Evelyn F. McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging.

d. November 11, 2016—Memorandum of Understanding amended the operation and management of the CAM-CTRP as follows:

- Transferred the CAM-CTRP from the Department of Geriatric Research on Aging at the Institute on Aging to the UF Department of Clinical and Health Psychology in the College of Public Health and Human Performance.
- Transferred the three faculty members in the CAM-CTRP to the Department of Clinical and Health Psychology in the College of Public Health and Human Performance.
- Created a Center for Cognitive Aging and Memory Clinical Translational Research (The CAM Center).
- Renovated space in the McKnight Brain Institute for the location of the CAM Center.
- Continued the funding of the CAM-CTRP through the CAM Center via the equal division of the investment income from McKnight Cognitive Aging Research Grant Fund for continued funding of the Age-Related Memory Loss research programs in the MBI.

e. February 1, 2017--Amended and Restated Memorandum of Understanding dated Nov. 11, 2016, the Center for Cognitive Aging and Memory Clinical Translational Research (the CAM Center) was approved by the University of Florida.

- The CAM Center was located in space in the Evelyn F. and William L. McKnight Brain Institute and was identified as the Center serving all the colleges within the UF Health Science Center.
- Ronald A. Cohen, PhD, was named Director of the CAM Center.

1.e. University of Florida – Gift Agreements, Continued

- The funding for the CAM Center was for the CAM-CTRP which resided within the CAM Center under the direction of Dr. Cohen.

f. July 22, 2019—Jada Lewis, Ph.D. professor in UF's department of neuroscience is appointed deputy co-director of the MBI

g. November 20,2022— The MOU dated November 11, 2016, was amended to move the Cognitive Aging and Memory Research Program primarily devoted to basic science research operating within the MBI to the Center for Cognitive Aging and Memory Clinical Translation Research along with the Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP). See Schematic. November 11, 2016.

- Transfer the Age-Related Memory Loss (ARML) Core Program from the MBI-UF to the Center for Cognitive Aging and Clinical Translational Research (the CAM Center) as a collaborating partner with the Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP) in the CAM Center.
- Name separate Co-Directors of the CAM Center for the administration of the ARML Core Program and the CAM-CTRP.
- Maintain the level of financial and infrastructure support through the CAM Center for the CAM-CTRP and the ARML Core Program currently in place.
- Develop complementary and collaborative research and educational programs between the ARML Core Program and the CAM-CTRP within the CAM Center intended to:
    1. Maintain and grow the research infrastructure for conducting cutting-edge discovery based cognitive aging research.
    2. Recruit, train and retain high-caliber young scientist interested in neural mechanisms for cognitive aging.
    3. Expand the scientific community at UF pursuing research relevant to age related cognitive decline and memory loss.
    4. Increase visibility of the research and develop messaging at local, national, and international level.
    5. Increase interactions and cohesion within the CAM Center, other UF Centers and industry partners to facilitate bidirectional (discovery to translation) cognitive aging and memory research at UF.
    6. Increase interactions with the other McKnight Brain Institutes and increase visibility of ARML Core Programs.
- Dr. Ron Cohen representing the CAM-CTRP and Dr. Jennifer Bizon representing the Age-Related Memory Loss research program in the MBI were named Co-Directors of the Center for Cognitive Aging and Clinical Translational Research (the CAM Center).
- Adam Woods, PhD, was named Assistant Director of the CAM-CTRP and Sara Burke, PhD, was named Assistant Director of the Cognitive Aging and Memory Program within the CAM Center

h. July 31, 2022--Todd E. Golde, MD, Ph. D resigns as Director of MBI to accept a position at Emory University.

i. February 23, 2023—Jennifeer Bizon, PhD was appointed Director of the MBI.

j. March 7, 2023---Sara Burke, PhD was appointed co-director replacing Dr.Bizon.

k. July,1, 2023—Dr. Ron Cohen was named as Professor Emeritus and resigned his position as assistant director.

l. March 23, 2023—Eric Porges, PhD replaced Dr. Bizon as co-director for collaborative research.

m. June 23, 2023—Adam Woods, PhD was named co-director replacing Dr. Cohen.
n. June 19, 2024---Adam Woods, PhD leaves UF to accept a position at UT Dallas.
o. October 7, 2024--- Sara Burke, Ph.D., who previously served as the center's co-director since March 2023 was named Director. The following additional appointments were announced.

- Eric Porges, Ph.D., associate director for collaborative resources (previously co-director).
- Natalie Ebner, Ph.D., associate director for faculty engagement and the Luttge Lecture series.
- Aprinda I. Queen, Ph.D., assistant director for computing and informatics.

2. Directors and Endowed Chairs:
   a. Founding Executive Director: William G. Luttge, Ph.D.—1995-1998 (Lectureship was funded in 2012).
   b. Executive Director: Todd E. Golde, MD, Ph.D.—2016—July 31, 2022.
   c. Interim Executive Director & Deputy Director: Steven T. DeKosky. M.D.—February, 2023.
   d. Co-Deputy Director: Jada Lewis, Ph.D., 2019—present.
   e. Director-Jennifer Bizon, PhD—Chair of the department of Neuroscience at UF was appointed Director of the MBI. February 2023.
   f. Steven T. DeKosky, MD remained Deputy Director of the MBI.
   g. Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging: (Valued at $4 million).
      - Thomas C. Foster, Ph.D.—2003—present
   h. Evelyn F. McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging: (Valued at $4 million). (Limited to five-year term, but renewable with mutual agreement, between MBRF and the UF).
      - Ronald A. Cohen, Ph.D.—2015—Renewed August 2020; Resigned and named Professor Emeritus July 2023, (Now vacant-recruitment underway)
   i. Center for Cognitive Aging & Memory Clinical Translational Research (The CAM Center)
      - Co-Director, Ronald A. Cohen, Ph.D.—2015— 2023 Clinical Translational Research Program in CAM Center.
      - Co-Director, Jennifer L. Bizon, PhD—2020—February 13, 2023 (When named Director of the MBI) (Age Related Memory Loss Program in CAM Center).
      - Co- Director—Sara Burke, PhD—March 2023-October 7, 2024.
      - Director, Sara Burke, PhD—October 7, 2024—Present.
      - Co-Director, Adam Woods, PhD, June 2023-June 19, 2024
      - Current Leadership of the CAM Center. **(See Section "1.o." above)**

D. University of Miami (UM)

1. Gift Agreements

a. December 24, 2006-- Gift Agreement provided for a gift of $5 million from the MBRF matched by the University of Miami (UM) over a five- year period of time.
The agreement also:
- Established the Evelyn F. McKnight Center for Age-Related Memory Loss.
- The UM agreed to recruit, through a national search, a qualified research scientist as a scientific director.

1.a. University of Miami ---Gift Agreements continued.

- Created a Director of Education position who would be responsible for developing clinical and post graduate training programs in cognitive aging and age-related memory loss.
- The UM agreed to recruit a qualified individual to occupy the Director of Education position.

b. December 10, 2010—Name Changed from "Center" to the Evelyn F. McKnight Brain Institute at the University of Miami.

c. February 9, 2011—Memorandum of Understanding between the UM and the MBRF to which the UM agreed to contribute from other sources the amount of investment income which would have been distributed in each respective year until the match was completed by the UM. (Note: Match was completed by the UM in 2013)

d. December 2012 -- Richard Isaacson, MD, resigned as faculty member and director of the education program to become Director of the Alzheimer's Prevention Clinic and faculty member in the Department of Neurology at Weill Cornell Medicine and New York-Presbyterian Hospital.

e. December 2013 -- UM match obligation completed as defined in the 2002 Gift Agreement with gifts of $1.8 million from the Schoninger Family designated for memory and aging disorders and the Di Tuillo Trust in the amount of $400,000 for cognitive research.

f. August 22, 2014—Gift agreement amended as follows:

- Established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $4 million, ($2 million from the MBRF and $2 million from UM).
- The MBRF funded the $2 million over three years, completing the gift in 2016.
- The UM match of $2 million was completed August 22, 2014.
- Clinton Wright, MD, the scientific director of the Evelyn F. McKnight Brain Institute at the University of Miami was named the first Evelyn F. McKnight Chair.
- The $4 million-dollar endowed chair was funded with $2 million dollars from the UM or donors to be match by the MBRF with $2 million, funded over a two-year period concluding 9/30/2016.
- August 22, 2014—University of Miami completed its match requirement for funding the Evelyn F. McKnight Endowed Chair.

g. October 2014—Xiaoyan Sun, MD, Ph.D, was named Director of Education.

h. October 31, 2016—Dr. Clinton Wright resigned as Scientific Director of the Evelyn F. McKnight Brain Institute at the University of Miami.

i. October 31, 2016—Tatjana Rundek, MD, PhD, was named Interim Scientific Director of the Evelyn F. McKnight Brain Institute at the University of Miami.

j. December 21, 2017—Dr. Tatjana Rundek, MD, PhD, was named the Scientific Director of the Evelyn F. McKnight Brain Institute and Evelyn F. McKnight Chair for Learning and Memory in Aging at the University of Miami after a nationwide search.

k. October 31, 2018—Dr. Tatjana Rundek, MD, PhD, was formally installed as the Evelyn F. McKnight Chair for Learning and Memory in Aging at the University of Miami with President Julio Frank, MD, PhD, MPH and Henri Ford, MD, MPH, Dean of the Miller Miami School of Medicine presiding with the trustees and colleagues in attendance.

1.l. University of Miami---Gift Agreements. continued

l. October 23, 2019—The trustees approved proposal to fund the one-time funding in the amount of $200,000 to launch the *Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship*. The grant is for $100,000 annually for a period of two years for a total not to exceed $200,000.

m. October 28, 2021—The trustees approved one-time funding for the *Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging* postdoctoral training program in the amount of $250,000 to be matched by the University of Miami. The grant is for $50,000 annually for a period of five years for a total not to exceed $250,000 with the understanding recruitment for the scholars will be from a national qualified applicant pool and efforts would be made to retain the successful scholars as clinical science faculty.

n. May 1, 2022—James. E. Galvin, MD, MPH, a renowned neurologist with strong research interest in cognitive aging and memory disorders was appointed as the Chief of the Cognitive Aging Division and the Alexandria and Bernard Schoninger Endowed Chair in Memory Disorders. Dr. Galvin will also serve as Director Comprehensive Center for Brian Health in expanding the UM MBI clinical neurology and cognitive services.

2. Directors and Endowed Chairs:

a. Executive Director: Ralph Sacco, M.D.—2007—deceased, January 17, 2023*
b. Scientific Director: Clinton B. Wright, M.D.—2007-2016
c. Interim Scientific Director: Tatjana Rundek, M.D., Ph.D.—2016—2018
d. Scientific Director: Tatjana Rundek, M.D., Ph.D. 2018—present*
e. Evelyn F. McKnight Endowed Chair for Learning and Memory in the Aging:
   - Clinton B. Wright, M.D.— 2014-2016;
   - Tatjana Rundek, M.D., Ph.D. 2018—present
f. Alexandria and Bernard Schrodinger Endowed Chair in Memory Disorders.
   - James E. Galvin, MD, MPH—installed February 21, 2023

*With Dr. Sacco's impending death due to an aggressive brain cancer, Dr. Henri Ford, Dean of the Miami Miller School of Medicine appointed **Dr. Rundek to occupy both the positions of Scientific Director and Interim Executive Director until the leadership of department of neurology could be identified since Dr. Sacco was also the Chair of the Department.** With the approval of the MBRF the position of the Scientific Director will be abolished and Dr. Rundek will assume the position of Director of the MBI at UM with the appointment of an associator director when the leadership is established similar to the governance models of each of the other MBIs.

g. July 8, 2024---Jose Romano, MD, national leader in vascular neurology research was named the chair of the department of Neurology at the University of Miami (UM) Miller School of Medicine.
h. July 8, 2024---Tatjana Rundek, MD, PhD. officially assumed the Director position of the UM Evelyn F. McKnight Brain Institute (EMBI). At the same time, Bonnie Levin, PhD, and Ihtsham Ul Haq, MD, as Co-Associate Directors of the University of Miami EMBI.

McKnight Leadership Council
February 2025

Arizona
Carol Barnes, Ph.D.
Director; Endowed Chair
carol@nsma.arizona.edu

Lee Ryan, Ph.D.
Associate Director
ryant@arizona.edu

Assistant
Peggy Ann Nolty
panolty@arizona.edu
520-626-2312

Kristina Irwin
kbirwin@email.arizona.edu
520-626-4571

Miami
Tatjana Rundek, M.D., Ph.D.
Director, EMBI; Endowed Chair
TRundek@med.miami.edu

Bonnie Levin, Ph.D.
Co-Associate Director, EMBI
blevin@med.miami.edu

Itsham Ul Haq, M.D.
Co-Associate Director, EMBI
ihaq@med.miami.edu

Assistant
Linda Beasley
lbeasley@med.miami.edu
305-243-1664

Alabama
Ron Lazar, Ph. D.
Director, EMBI, Endowed Chair
rlazar@uabmc.edu
Phone: 205-975-4955

Kristina Visscher, Ph,D.
Associate Director, EMBI
kmv@uab.edu

Assistant
Tanji Stephens
tstephens@uabmc.edu
205-996-5875

Florida
Jennifer L. Bizon, Ph.D.
Director, EMBI
bizonj@ufl.edu

Sara N. Burke, Ph.D.
Associate Director of the Cognitive Aging &
Memory Center
burkes@ufl.edu

Assistant
Brittany Zabel
Zabel.brittany@ufl.edu

Leadership Council: carol@nsma.arizona.edu; ryant@email.arizona.edu; bizonj@ufl.edu; steven.dekosky@neurology.ufl.edu; roncohen@ufl.edu; rsacco@med.miami.edu; TRundek@med.miami.edu; rlazar@uabmc.edu; dstandaert@uabmc.edu; eroberson@uab.edu

cc: kbirwin@email.arizona.edu; fmorris@med.miami.edu; lbeasley@med.miami.edu; tstephens@uabmc.edu; calewi@uabmc.edu; cchambless@uabmc.edu; sabrina.sanchez@mbi.ufl.edu; tinalacy@ufl.edu; pjoy@ufl.edu; panolty@arizona.edu

McKnight Brain Research Foundation (MBRF)

Annual Report
Sponsored Institutes and Research Programs
(Include activity of all McKnight supported faculty and trainees)

Some gift agreements require Institute reports, Center Directors, and Chair reports.
If applicable, please clearly state whether a particular response relates to a Chair, Center or Institute.

Submitted by:_____

Report Period:_____

Please provide an easy to read, easy to evaluate summary of your MBI's activities, focusing on those that are new since last year's report. Please be succinct and focus on activities and accomplishments relevant to the McKnight Brain Research Foundation, i.e., age-related cognitive decline and memory loss. No item should be included in more than one section. Please spell out acronyms with first use when not universally understood.

1. Table of Contents

2. Letter from the Director(s). This signed and dated letter should summarize the current focus of the MBI, highlights and challenges of the past year, and major plans for the upcoming year.

3. Include a separate letter from each McKnight Chair, Center Director, or Chairholder if the Chairholder is not the Institute Director.

4. Institute FY24 at a Glance (Please include only items relevant to the MBRF's mission related to age-related cognitive decline and memory loss)

    - Summary of major scientific, programmatic, outreach or training achievements since last year, including clinical, translational programs, and educational programs

    - Identify and include what you consider the most important, relevant scientific achievement(s) of the past year

    - Provide the current MBI budget and an Endowment Investment Report

5. Collaborative Programs with McKnight Institutes and non-McKnight Institutes

(Please reference any collaborative programs that are included in detail in Section 3. Please note, if the Principal Investigator of a collaborative study works within your MBI, please include an overview of the research being conducted in the collaborative study and include the names and affiliations of other collaborators.)

6. Honors, Awards and New Grants

7. Technology transfer (Patents/applications; Revenue generated from technology)

8. Were any funds used for a Prohibited Purpose during the report period?

9. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

10. Did all activities during the report period further the Purpose?

11. Additional Comments (items that are not covered elsewhere in the report, including any negative events, loss of full-time employees (FTEs), impending departures, space, or budget that could have an impact on carrying out the Gift Agreement.)

Signature (date, and title of person submitting the report)

Appendices

12. Appendix 1
    List of McKnight Affiliate Faculty and their area of focus, and Department Affiliations, including a list of post-doctoral and pre-doctoral trainees (CVs needed only for new faculty/collaborators)

13. Appendix 2
    List up to 20 publications from FY24 relevant to the MBRF

14. Appendix 3
    Top 10 presentations at scientific or public meetings relevant to the MBRF

15. Appendix 4
    Highlights of website development, media coverage and/or social media audience development

16. Appendix 5
    Please use the attached form to summarize the number of collaborations with MBIs, Collaborations with non-MBIs, Awards & Honors, Grants, Top Publications, Members (Faculty, Collaborators/Affiliates, and/or Trainees, as specified)

17. Appendix 6
    Please provide an organizational chart for the MBI.

PLEASE POST YOUR REPORT (EXCLUDING FINANCIAL INFORMATION) ON YOUR WEBSITE.

Annual Report

McKnight Brain Research Foundation
Sponsored Institutes and Research Programs
(Include activity of all McKnight supported faculty and trainees)
Report Period: _____

Financial Summary Format

_____(Institute)_____

Summary for 12 months ended _____

Account Name: _____

A.	Beginning Balance on _____	$ _____
B.	Investment Growth	$ _____
C.	Distributions	$ _____
D.	Additional Contribution	$ _____
E.	Ending Balance on _____	$ _____
F.	Unmatched Balance (if applicable)	$ _____

DEFINITIONS

DISTRIBUTION is the money transferred from the account to the spendable/operating account for the designated use.

BALANCE is the market value of the account as of the first or last day of the reporting year.

ADDITIONAL CONTRIBUTION is additional contribution by MBRF, the reporting institution, match etc.

INVESTMENT GROWTH (Loss) is the total undistributed interest, dividends, and realized and unrealized gains and losses.

BALANCE is the value of the account's corpus including all contributions, and applicable state match monies as of the date indicated.

Appendix 5

Collaborations with MBIs	Collaborations with non-MBIS	Awards and Honors	Grants	Top Publications	Members (Faculty, Collaborators/Affiliates, and/or Trainees, as specified)
		Total # of awards and honors # Senior Faculty # Junior Faculty	Total # of new grants # Senior Faculty # Junior Faculty		# - Leadership and Members # - Collaborators # Trainees

MBRF Block Grants
and
Special Projects

McKnight Brain Research Foundation (MBRF) Block Grants, Pilot Grants, and Special Projects

1. October 22, 2009—A Travel Award Program was approved by the MBRF Trustees. The Trustees established a travel award fund of $100,000 to support travel of research scientists to other McKnight Brain Institutes (MBIs) for educational purposes or to convene focus groups between MBIs to develop collaborative research programs.

2. 2012-2016—Cognitive Aging Core Working Groups were funded through the Travel Award Program. The five (5) working groups and their focus areas are as follows:

A. Brain and Cognitive Health Core Working Group
- Supports collaborative discussions to develop strategies to promote brain and cognitive health.

B. Cognitive Aging and Memory Interventional Core Working Group
- Supports collaborative discussions with the objective to accelerate clinical translation of interventions for alleviating cognitive aging and memory decline in older adults and to identify promising new cognitive aging interventions that could be rapidly implemented across the McKnight Brain Institute network and beyond.
- Supports the design, development, implementation and dissemination of multidisciplinary interventions for improved cognitive health as a necessary future direction.

C. Cognitive Testing Battery Core Working Group
- Supports collaborative discussion on the adoption of common standards of cognitive tests which then would become common standards between investigators.

D. Epigenetics Core Working Group
- Supports discussions on development of a broad collaborative initiative to propel discovery and advancement concerning the role of epigenetic mechanisms and processes in memory and cognitive aging.

E. Magnetic Resonance Imaging (MRI) Standardization Core Working Group
- Supports collaborative working group to standardize the MRI data between the McKnight Brain Institutes and the calibration of the equipment at each MBI for consistency of results.

3. Several grants were funded by the MBRF Trustees after recommendation by the Core Working Groups. They are as follows:

A. September 1, 2013—Inter-Institutional Bio-Informatics Core--$600,000 ($300,000 for two years) funded upon recommendation by the Epigenetics Core Working Group. The two-year grant was approved to establish a comprehensive program to test an epigenetic hypothesis of cognitive aging, working collaboratively with all the McKnight Brain Institutes with the goal to establish a shared Inter-Institute resource to provide a catalyst for discoveries in the area of epigenetics of cognitive aging. This is envisioned to be a "core without walls" to provide support for bioinformatic analysis of high-throughput DNA/RNA sequencing and epigenomics, bioinformatics, and cross-correlation of human and animal studies.

- Principal Investigators:
  Dr. Matthew Huentleman, UA
  Dr. David K. Sweatt, replaced by Dr. Jeremy Day, UAB
  Dr. Tom Foster, UF

B. January 1, 2015—Inter-Institutional Neuroimaging Core--$931,759 (Two-year award) The two-year grant was approved upon recommendation by the MRI Standardization Core Working Group to establish and standardize a common neuroimaging protocol across all four McKnight Brain Institutes to develop a Cognitive Aging Assessment Core and a McKnight Brain Aging Registry of the oldest old. The purpose of the grant is to collect comprehensive data on brain morphology and function, cognition, and vascular risk, on participants 85 years and older, to support proposals for translational research to the NIH and other funding sources to identify and evaluate effective interventions for age-related memory loss.

- Principal Investigators:
  Dr. Kristina Visscher, UAB
  Dr. Gene Alexander, UA
  Dr. Norm Halprin, UM
  Dr. Ron Cohen, UF

C. September 1, 2015--Inter-Institutional Cognitive Assessment and Brain Registry Core Award: $800,000 ($400,000 per year for two years) The funding request was approved upon the recommendation by the Brain and Cognitive Health Core Working Group. The purpose of the two-year grant is to establish and develop McKnight Cognitive Aging Assessment Core as a companion to the Inter-Institutional Neuroimaging Core to provide supplemental cognitive testing to acquire comprehensive cognitive, behavioral, and relevant clinical data on older adults over the age of 85 to complete the Brain Aging Registry which would contain both the MRI and Cognitive assessment data.

- Principal Investigators:
  Dr Virginia G. Wadley, UAB
  Dr. Gene Alexander, UA
  Dr. Ron Cohen, UF
  Dr. Bonnie Levin, UM

4. July 16, 2016—The Trustees approved a proposal from the MBRF Clinical Translational Working Group to establish a "Cognitive Aging and Memory Intervention Core" without a budgetary requirement. The purpose of the Cognitive Aging and Memory Intervention Core is to create a high profile nationally recognized interventional hub for the four MBIs and to complement the existing Brain Aging Registry, Cognitive Assessment Core, and Epigenetics Core. The Cognitive Aging and Memory Intervention Core will identify research programs for collaborative potential between the four MBIs and solicit pilot grant proposals which would be reviewed by the Cognitive Aging and Memory Intervention Core. If approved by the core committee, the pilot grant proposal would be forwarded to the research committee of the MBRF and ultimately to the MBRF Trustees for review and funding consideration. The first Pilot Grant Program Awards were made in 2018 with the goal that these pilot research grant initiatives would position them for additional funding by the NIH or other sources.

Pilot Grant Awards:

A. June 1, 2018-- Vulnerability of Older Adults to Financial Deception Schemes—A Novel Intervention Tool--$60,000 per year for two years. The proposal will involve collaboration from investigators from three MBI sites and is designed to test intervention to reduce susceptibility to financial scams in older adults. Specifically, it is anchored in the important social and cognitive issues associated with age-related cognitive decline and memory loss. The proposed study would develop a prototype scam detection intervention software which would be used in the future to assist seniors in recognition and prevention from being scammed.

- Principal Investigators:
  Dr. Bonnie Levin, UM
  Dr. Sarah Getz, UM
  Dr. Robert Wilson and Dr. Matthew Grilli, UA
  Dr. Natalie Ebner and Dr. Daniella Oliveira, UF (Dr. Oliveira withdrew in July 2020)

B. June 1, 2018—A Pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults. --$60,000 per year for two years. The study involves collaboration between investigators from two McKnight Brain Institute sites. The goal of the study is to evaluate the potential of near infrared non-invasive brain stimulation for remediating age-related cognitive decline. The study proposes a neuromodulation method that is highly novel based on the use of infrared light to impact underlying mitochondrial activity in the brain. The proposed mechanism of action differs from other non-invasive neuromodulation approaches that focus on neuroplasticity (e.g.), transcranial direct current stimulation).

- Principal Investigators:
  Dr. Dawn Bowers, UF
  Dr. Adam Woods, UF
  Dr. Gene Alexander, UA

C. July 31, 2019-- Transcutaneous Vagal Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults--$60,000 per year for two years., beginning October 1, 2019. The study is designed to evaluate the pairing of cognitive training and non-invasive neurostimulation technology that has shown promise in both increasing neuroplasticity and in enhancing cognitive performance through transcutaneous vagal nerve stimulation.

- Principal Investigators
  Dr. John B. Williamson, UF
  Dr. Gene Alexander, UA
  Dr. Ronald A. Cohen, UF
  Dr. Damon Lamb, UF
  Dr. Eric Porges, UF
  Dr. Adam Woods, UF

5. October 23, 2019—Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship Program for $200,000 ($100,000 per year for two years with starting date July 1, 2020) The MBRF Trustees approved the request from the Evelyn F. McKnight Brain Institute (MBI) at the University of Miami (UM) to support a fully funded two-year post-doctoral clinical fellowship dedicated to study age-related cognitive decline and memory loss. The MBRF Trustees approved funding as inaugural funding for the two-year clinical fellowship with the expectation that the MBI at the University of Miami would secure funding from other sources or provide the funding after 2022.

- Evelyn F. McKnight Neurocognitive Scholar:
  Christian Agudelo, M.D., was named the Evelyn F. McKnight Neurocognitive Scholar in March of 2020, starting his position in July 2020.

6. February 5, 2020—Supplemental Grant Award, Precision Aging Project, U-19 Proposal--$244,400. In 2019, Dr. Carol Barnes, director of the MBI at UA submitted a proposal to the National Institutes of Health for a U19 grant entitled **"Precision Aging Network: Closing the Cognitive Healthspan, Human Lifespan Gap".** The proposal was an enormous undertaking, with ~40 individuals

6. Continued…

participating. The proposal was reviewed by NIH, but Dr. Barnes, the PI of the U19 grant, and the associate directors of the grant, were notified additional intake information on the different demographic of participants (Spanish speaking cohort).in the study was required. The PI was also informed that application could be made for pilot support from his Strategic Initiative fund to mount a study to collect preliminary data for the U19 resubmission. The University of Arizona has contributed some matching funds to support the pilot project, but the supplemental pilot project was to be performed at the UM MBI for which there are no budget funds. Because of the importance and magnitude of the Precision Aging U-19 grant proposal and its potential contribution to the understanding and alleviation of age-related cognitive decline and memory loss, the Trustees approved the request for $244,400 to support the supplemental project to the Precision Aging U-19 Grant.

7. February 26, 2021--Harnessing Optimal Mechanisms of Exercise for Cognitive Gains (HOME-Cog) -- $60,000 per year beginning May 1, 2021. The current proposal outlines a collaborative project between the Evelyn F. McKnight Brain Institutes (MBI) at University of Miami and University of Florida that aims to inform the knowledge gap on the mechanistic action of exercise on the brain by characterizing important mechanisms of neuroplasticity and cardiovascular capacity, proposed to underlie cognitive response to exercise.

- Principal Investigators
  Joyce Gomes-Osman, PT, PhD, UM
  Katalina McInerney, PhD (Co-Investigator), University of Miami
  Mitchell Slugh, PhD, (Co-Investigator University of Miami
  Tatjana Rundek, MD, PhD (Co-Investigator), University of Miami
  Bonnie Levin, PhD (Co-Investigator), University of Miami
  David Loewenstein, PhD (Co-Investigator), UM
  Alvaro Pascual-Leone, MD, PhD (Co-Investigator), Professor of Neurology, Harvard Medical School
- Collaborators
  Eric Porges, PhD, UF
  Joseph Gullett, Research Assistant Professor, UF
  Adam Woods, PhD, UF
  Ronald Cohen, PhD, UF

8. February 26, 2021--Improving Age-Related Cognitive Decline with Exercise in Hypertensive Older Adults: A Pilot Study to Investigate a Retinal Microvascular Biomarker and the Role of IGF-1--$56,144 per year for two years. The study is designed to examine the relationship of retinal microvascular density, IGF-1 and cognitive function in older individuals with essential hypertension. The goal of the study is to determine whether an exercise intervention will improve age-related growth factor deficiencies and retinal microvascular density, and, in turn, be associated with an improvement in cognition

- Principal Investigator
  Ronald M. Lazar, PhD (UAB)
- Collaborators
  Christopher Girkin, MD, MSPH (UAB)
  Marcas Bamman, PhD (UAB)
  Tatjana Rundek, MD, PhD (UM)
  Jianhua Wang, MD, PhD (UM)

9. September 28, 2021—The Precision Aging Network: "**Closing the Cognitive Healthspan, Human Lifespan Gap"** grant submitted by Dr. Carol Barnes, Director of the Evelyn F. McKnight Brain Institute at the University of Arizona has been awarded a five-year $60 million grant from the National Institutes of Health to create and lead that could transform the way we think about the aging brain. Dr. Barnes will lead the network and bring together researchers from across the country to better understand how and why people experience brain aging differently, with the ultimate goal of developing more effective treatments and interventions targeted to the individual.

10. January 3, 2022-- The McKnight Brain Aging Registry (MBAR) study has completed all recruitment and assessments with over 200 participants who are over 85 years. Extensive quality control and validation of the database has occurred with one manuscript under review, three others to be submitted soon, and multiple others in 49 the works. MBAR cognitive, neuroimaging and biomarker data are available upon request to the MBAR Scientific Advisory Committee. The request form will be hosted on the CAM center website. A funding balance of the $88,519.11 remains in the account.

11. January 22, 2022—The leadership of the Cognitive Aging and Memory Intervention Core (CAMI) changed and reported only one application for the 2022 awards cycle. Several reasons were cited including the influence of the pandemic and a request to amend the criteria described in the Request for Applications should be modified.

12. February 22, 2022, the leadership if the CAMI were notified the request for the RFA was denied and recommendations for restructuring the committee redefining Pilot Grant Program thought collaborative discussions between MBRF leadership with members of the Leadership Council composed of the representatives of the four MBIs. The deadline for application under current RFA criteria was extended to May1, 2022.

13. May 1, 2023 --"Feasibility of a Timed Bright Light Exposure Therapy to Improve Circadian Function". The purpose of the study is to examine the feasibility and tolerability of timed bright light exposure therapy to enhance circadian function in the oldest old. Award: $60,000 per year for two years.

- Principal Investigators
  Sonya Kaur, PhD
  Karem Gamble, PhD
- Mentors
  Bonnie Levin, PhD
  Alberto Ramos, PhD

14. May 1. 2023--Ketogenic Diet Improvement of Age-Related Memory Impairments, Nominates Cell-type Specific O-GicNAc Deficiencies in the Aged Hippocampus". The study is designed to investigate the contribution of metabolic O-linked N-acetylglucosamine (O-GlcNAc). The research is targeted toward gaining a greater understanding of the underlying metabolic mechanisms involved in the benefit of Ketogenic diet therapy on improvement of memory impairments associated with age. Award: 2 years. Year 1: $53,434; Year 2: $64,391.

- Principal Investigator
  Farah D. Lubin, PhD
- Co-Principal Investigator
  Matthew Huentelman, Ph.D.

15. May 1, 2023 -- "Cued High-Speed Multidirectional Yoga: Impact on Retinal Microvascular and Cognitive Measures". The proposed YogaCue program includes high-speed intervals to address cardiovascular fitness, and multi-directional responses to visual and auditory cuing, with pattern recognition and retention to address multiple cognitive domains. We will use changes in the retina

microvasculature and capillary function and targeted cognitive testing to assess the success of the Yoga Cue program. Award: 2 years; Year 1: $59,997; Year 2: $59,742

- Principal Investigator
  Joseph F. Signorile, PhD
- Co-Principal Investigators
  Jianhua Wang, MD, PhD; Hong Jiang, MD, PhD, and Natalie Ebner, PhD,

16. April 25, 2024—The McKnight Brain Aging Registry (MBAR) was approved. The McKnight Brain Aging Registry (MBAR) study was completed in January 2022 of all recruitment and assessments with over 200 participants who are over 85 years. Since completion of the study the MBAR cognitive, neuroimaging, and biomarker data have been available upon request. The overarching goal of the proposal is to use the exiting funds of $88,519.11 to maintain active data sharing throughout the four MBIs to distribute workable/easy to analyze versions of datasets from the MBAR to research scientists who will use it for 1) analysis to create impactful peer-reviewed research papers, 2) preliminary data for future grant proposals. These datasets have been instrumental for several current projects across the MBIs and have the potential to launch further projects. The approval is for two years with annual reports and a total budget of $88,530.

17. April 25, 2024—The revised request proposal for Request for Application for Pilot Grant Awarded through the Cognitive Aging and Memory Intervention Core (CAMI) was approved by the Trustees with the following new review committee membership.

- Sara Burke, Chair burkes@ufl.edu (UF)
- Ihtsham ul Haq ihaq@med.miami.edu (U Miami)
- Matthew Grilli mdgrilli@arizona.edu (UA)
- Keith McGregor kmmcgreg@uab.edu (UAB

18. February 24, 2025--**Reduction in alcohol consumption on cognition in normal aging.**
This grant proposal aims to explore the potential effects of probiotics in conjunction with alcohol cessation behavioral training among older adults who are classified as high-risk drinkers. The study plans to enroll 20 participants who do not have diabetes and will be randomized into either a probiotic group or a placebo group. At baseline and after 30 days, participants will undergo brain imaging using deuterium metabolic spectroscopy (DMT) to assess glucose metabolism in specific brain regions, notably the medial frontal area, as well as cognitive performance evaluations focusing on fluid cognition.

- Principal Investigator(s):
  Teddy Salan, PhD (U Miami) (Early-stage/New Investigator)
  Eric Porges, PhD (UF)

19. February 24, 2025**—Novel approaches to cognitive interventions that target navigation skills in healthy older adults.** This grant proposal aims to investigate the impacts of two distinct interventions—navigation training and useful field of view (UFOV) training—on spatial navigation and orientation declines in cognitively normal older adults.

- Principal Investigator(s):
  Contact PI: Arne Ekstrom, PhD, University of Arizona, Professor
  Co-PI – Steven Weisberg PhD, University of Florida, Assistant Professor
  Co-I – Paul Hill PhD, University of Arizona, Research Scientist
  Co-I – Natalie Ebner PhD, University of Florida, Professor (Psychology)
  Co-I – Kristina Visscher PhD, UAB, Associate Professor (Neurobiology)

20. February 24, 2025**—Effects of age on fear generalization and its underlying neurobiological substrates in female adults: a cross-species investigation.** This grant proposes to address critical gaps in our understanding of how aging impacts fear, learning, and memory, specifically focusing on fear generalization in older women and female rats.

- Principal Investigator(s):
  Co-PI – Ashley Huggins, PhD, University of Arizona
  Co-I – Caesar Hernandez, PhD, University of Alabama, Birmingham

McKnight Brain Research Foundation Inter-Institutional Meetings

- Annual meeting of all research scientists from each of the four McKnight Brain Institutes

- The role of host of the inter-institutional meeting rotates among the McKnight Brain Institutes annually.

- The Annual cost of the meeting is supported by McKnight Brain Research Foundation.

- Annual Budget: $100,000 plus Trustee travel and meeting expenses*

- **2008:** 1st meeting hosted by Evelyn F. McKnight Brain Institute at the University of Arizona

- Cognitive Aging Summit IV symbolizes the 15th anniversary of the Inter-inter-institutional meetings

- **15th** Inter-institutional meeting was held **May 15-17, 2024**, and was hosted by the William L. and the Evelyn F. McKnight Brain Institute of the University of Florida

Draft 2024 Inter Institutional Meeting Agenda.pdf

https://mbi.ufl.edu/2024/05/20/mcknight-brain-research-foundation-meeting-convenes-top-cognitive-aging-researchers/

* Because of inflationary pressure, in 2023 the budget was approved not to exceed $130,000.

16th Annual Inter-Institutional Meeting
Evelyn F. McKnight Brain Institutes
McKnight Brain Research Foundation and University of Miami MBI
MAY 14 - 16, 2025

BRAIN HEALTH: From Discoveries to Community

DRAFT AGENDA February 12, 2025

Wednesday, May 14th, 2025

Location: **Nautilus Sonesta**
1825 Collins Ave
Miami Beach, FL 33139
Phone 305-503-5700

12:00pm - 5:00pm **PRE-MEETINGS**

12:00pm - 12:15pm Introduction to Pre-Meetings (Ihtsham Haq and Tatjana Rundek, UM)

12:15pm - 1:00pm Lunch

1:00pm - 2:00pm
1. Neuromodulation (*Chairs:* Eric Porges, UF; Keith McGregor, UAB)
2. Precision Aging (*Chairs:* Carol Barnes, UA; Ron Lazar, UAB)

2:00pm - 3:00pm
3. Metabolism & Cardiovascular Function (*Chairs:* Sara Burke, UF; Lee Ryan, UA)
4. Neuroinflammation (*Chairs:* Tom Foster, UF; Meredith Hay, UA)

3:00pm - 4:00pm
5. AI & Neuroimaging (*Chairs:* Ihtsham Haq, UM; Arne Ekstrom, UA)
6. Psychiatric Influences on Cognitive Aging (*Chairs:* Barry Setlow, UF; Bonnie Levin, UM)

4:00pm - 5:00pm **MCKNIGHT BRAIN AGING REGISTRY) (MBAR)** (*Chairs*: Kristina Visscher, UAB; Bonnie Levin, UM)
INTER-INSTITUTIONAL PROJECTS AND COLLABORATIONS (CAMI Core: Ihtsham Haq, UM; Sara Burke, UF)

5:00pm - 6:00pm **YOUNG INVESTIGATOR SESSION for Future Research Directions (confirmed for now)**
NIA/NINDS: Molly Wagster/Clinton Wright

6:00pm - 8:00pm **Dinner Reception**
Nautilus Hotel

6:15pm - 6:45pm **Welcome**
Tatjana Rundek, M.D., Ph.D.
Director of Evelyn F. McKnight Brain Institute

Guillermo (Willy) Prado Ph.D.
Interim Provost and Executive Vice President for Academic Affairs

Michael L. Dockery, M.D.
Chair, Board of Trustees, McKnight Brain Research Foundation

6:45pm - 8:00pm **Dinner**

8:00pm – 10:00pm **Activities**

Thursday, May 15th, 2025

Location:	**Nautilus Sonesta** **1825 Collins Ave** **Miami Beach, FL 33139** **Phone 305-503-5700**
8:00am - 8:45am	Breakfast
9:00am - 9:30am	**Welcome & Introduction**
	New Direction McKnight Brain Research Foundation **Michael L. Dockery, M.D.** Chair, Board of Trustees, McKnight Brain Research Foundation (MBRF)
	Jose Romano, FAHA, FAAN, FAAN Chairman, Department of Neurology U Miami
	Introduction to Program and Meeting Overview **Tatjana Rundek, M.D., Ph.D.** Director of Evelyn F. McKnight Brain Institute
	Introduction of the 1st Ralph L. Sacco Scholars in Brain Health by AAN/AHA (Dr. Patrick Devlin, UT Houston and Dr. Cyprien Rivier, Yale)

SESSION I	**Biomarkers of Optimal Aging: Potential Intervention Targets**
9:30am - 10:30am	**Moderators: Farah Lubin, UAB and Tom Foster, UF**
9:30am - 9:40am	Consequences of Mitochondrial Defects in Aging Neurons: Carlos Moraes (UM)
9:40am - 9:50am	Imaging and Epigenetic Biomarkers of Brain Health: Yenisel Cruz-Almeida (UF)
9:50am - 10:00am	Biomarkers of Sleep in Aging: Christian Agudelo (UM)
10:00am - 10:10am	Biomarkers: ……. (UAB) **Ron Lazar to add**
10:10am - 10:35am	**Pannel Discussion (Discussion Lead: Farah Lubin)**
10:35am - 10:45am	Break

SESSION II	**Translation to Practice and Community**
10:45am - 11:45am	**Moderators: Christian Agudelo, UM and Ron Lazar, UAB**
10:45am - 11:00am	Community Participatory Research: Rosie Curiel (UM)

11:00am - 11:15am	Caregiver Interventions for Aging in the Community: David Coon (UA)
11:15am - 11:30am	From Practice to Public Health: Cognitive Aging: Victor Del Bene (UAB)
11:30am - 11:45am	**Panel Discussion (Discussion Lead: Susan Fox Rosellini, UM)**

12:00pm - 2:00pm **LUNCH AND KEYNOTE LECTURE**
Brain Health: A Call to Action

Natalia S. Rost, MD, MPH, FAHA, FAAN
Professor of Neurology, Harvard Medical Center
Massachusetts General Hospital
President, American Academy of Neurology

SESSION III	**Environmental Challenges to Brain Health**
2:00pm - 3:00pm	**Moderators: Bonnie Levin, UM and Kristina Visscher, UAB**
2:00pm - 2:15pm	Harmful and Algae Blooms and Brain Health: Larry Brand (UM)
2:15pm - 2:30pm	PFAS and Brain Health: Hannah Gardener (UM)
2:30pm - 2:45pm	Environmental Challenges to Brain Health: Ashely Adamson (UAB)
2:45pm - 3:00pm	**Panel Discussion: (Discussion Lead: Bonnie Levin, UM)**
3:00pm - 3:15pm	Break

SESSION IV	**Machine Learning and Big Data Approaches to Cognitive Aging**
3:15pm - 4:00pm	**Moderators: Ihtsham Haq, UM and Aprinda Queen, UF**
3:15pm - 3:25pm	Digital Twin Approaches to Cognitive Aging: Yelena Yesha (UM)
3:25pm - 3:35pm	Imaging Analysis for Detecting Risk of Cognitive Decline: Josh Gullet (UF)
3:35pm - 3:45pm	Precision Aging at Scale: Clustering Cognitive Data for Personalized Interventions: Maisam Jafri (UA)
3:45pm - 4:55pm	**Title TBD** Junghee Lee (UAB)
3:55pm - 4:10pm	**Panel Discussion: (Discussion Lead: Ihtsham Haq, UM)**

SESSION V	**Brain Health: Action & Implementation (from pre-meeting groups)**
4:15pm - 5:30pm	**Moderators: Lee Ryan, UA and Jen Bizon, UF**
4:15pm - 5:00pm	Pre-Meeting Group Leaders Present Action Items and Next steps
5:00pm - 5:30pm	Discussion

5:40pm - 5:45pm	Board buses
6:00pm - 8:30pm	**Dinner at Joe's Stone Crab**

Friday, May 16th, 2025

7:30am - 8:30am	**Breakfast at Nautilus hotel**
	Board of Directors Breakfast with MBI Directors
8:30am - 8:45am	**Board buses to depart for UM starting at 8:15am**
Location:	**University of Miami** **Bascom Palmer Auditorium**
9:15am - 9:30am	**Introduction** **Henri R. Ford, M.D., MHA** **Dean and Chief Academic Officer** **University of Miami Leonard M. Miller School of Medicine**

SESSION VI **Translating Discoveries into Action**
9:30am - 10:30am **Moderators: Carol Barnes, UA and Tatjana Rundek, UM**

10 min. presentation with 5 min. for Q & A after each presentation

9:30am - 9:45am	Genetics of ApoE4 and Aging: Jeff Vance (UM)
9:45am - 10:00am	Aging Models: Raymond Jones (UAB)
10:00am - 10:15am	**Tite TBD:** Natalie Ebner (UF)
10:15am - 10:30am	Transcranial Magnetic Stimulation for Mild Cognitive Impairment and Alzheimer's Disease: Ying-Hui Chou (UA)
10:30am - 10:40am	Break

Session VII **Blitz Presentations**
10:40am - 11:45am **Moderators: Kristina Visscher, UAB and Sara Burke, UF**

5 min presentation with 2 min for Q & A after each presentation

DR. RUNDEK, 1 minute is allowed in between blitzes for switching speakers and putting presentations up.

10:40am - 10:47am	McKnight Brain Aging Registry (MBAR) Kristina Visscher, UAB to provide title
10:48am - 10:55am	McKnight Brain Aging Registry (MBAR) Eric Porges, UF to provide title
10:56am - 11:03am	Cognitive Aging and Memory Intervention (CAMI) Core Ihtsham Haq, UM to provide

11:04am - 11:11am	Cognitive Aging and Memory Intervention (CAMI) Core Sara Burke, UF to provide title
11:12am - 11:19am	Life Essential 8 and Cognition: Taly Elfassy (UM)
11:20am - 11:27am	**UA - TBD** on normative aging Matt Grilli, Ashley Huggins or Arne Ekstrom
11:28am - 11:35am	**UAB - TBD**
11:36am - 11:43am	**UF - TBD**
11:45am - 12:00pm	**Closing Remarks**
12:00pm	**Meeting adjourns** Lunch: Boxed lunches available for pickup on the way out

The Precision Aging Network
September 28, 2021

The Precision Aging Network: "**Closing the Cognitive Healthspan, Human Lifespan Gap"** grant submitted by Dr. Carol Barnes, Director of the Evelyn F. McKnight Brain Institute at the University of Arizona has been awarded a five-year $60 million grant from the National Institutes of Health to create and lead that could transform the way we think about the aging brain. Dr. Barnes will lead the network and bring together researchers from across the country to better understand how and why people experience brain aging differently, with the ultimate goal of developing more effective treatments and interventions targeted to the individual.

Research Partnership in Cognitive Aging

2009—The Research Partnership in Cognitive Aging between the National Institute on Aging (NIA) and the McKnight Brain Research Foundation (MBRF) was established to support the funding of competitive grant research proposals in cognitive aging through the Foundation for the NIH (FNIH).

- Agreement by the MBRF and the NIA was reached for each organization to provide a minimum of $1 million each for a period of five years to fund proposals for research in cognitive aging and age-related memory loss to be vetted by the NIA process and procedures.
- For the first five-year cycle the MBRF contributed $5 million and the NIA and other partners contributed $23 million.
- Requests for applications targeted two research areas:

  1) Interventions to remediate age-related cognitive decline

  2) Neural and behavioral profiles of cognitive aging

- 17 five-year research proposals were funded

2014 – The Research Partnership in Cognitive Aging was renewed

- Funded a five-year clinical trial *"Cognitive Decline: Mindfulness-based Stress Reduction and Exercise"*
- MBRF's contribution was $5 million; NIA's contribution was $15 million

2019 – The Research Partnership in Cognitive Aging was renewed

- Funded a five-year concept for development *"Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age."*
- The funding opportunity announcement has been posted on Grants.NIH.Gov. Letters of Intent were due September 1, 2020, and applications due October 1, 2020, but were delayed until May 2021, but was delayed until May 2021.

- MBRF's contribution: $5 million. The unofficial contribution from the NIA is expected to be a three for one match for a total of $15 Million from the NIA. Both MBRF and NIA contributions are payable over five years).

Research Partnership in Cognitive Aging

A report to the McKnight Brain Research Foundation

January 31, 2024

Foundation for the National Institutes of Health
National Institute on Aging

REPORT SUMMARY

The Foundation for the National Institutes of Health (FNIH) is pleased to present the following Research Partnership in Cognitive Aging 2023 report to the McKnight Brain Research Foundation (MBRF). The report provides an update from the National Institute on Aging (NIA) on the Cognitive SuperAgers Networks, both supported through the Research Partnership in Cognitive Aging. The report also includes updates on the Mindfulness, EDucation, and EXercise for Age-Related Cognitive Decline (MEDEX) trial (now complete) continuation study, as well as two additional initiatives that stemmed from the Cognitive Aging Summit III.

The current centerpiece of the Research Partnership in Cognitive Aging between the NIA and MBRF, coordinated by the FNIH, is the research supported through the funding opportunity "Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age," RFA-21-015 (https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-21-015.html). Updates to this research are provided below.

"Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age (U19 Clinical Trial Not Allowed)"

Resilience/Resistance to Alzheimer's Disease in Centenarians and Offspring (RADCO) U19AG073172

The RADCO cooperative agreement (U19AG073172), awarded to Drs. Thomas Perls (Boston University Medical Campus), Stacy Andersen (Boston University Medical Campus), and Susan Bookheimer (UCLA) is in the third year of award. The NIA is supporting a multi-year administrative supplement to enhance diversity and data capture, in the form of a fourth phenotyping and biospecimen core and neuroimaging core site at Georgia State University (GSU). The addition of the GSU site has enhanced the diversity of the RADCO cohort. The goal is to enroll 234 Black participants, thus increasing the Black participant proportion of the RADCO sample from 7.2% to 22.2%.

The abstract for U19AG073172:

DESCRIPTION (provided by applicant): Centenarians delay age-related diseases and disabilities into their mid-nineties. Some remain cognitively intact despite extreme exposure to the strongest risk factor for cognitive impairment and Alzheimer's disease (AD), aging. The overall hypothesis of this study, titled "Resilience/Resistance to AD in Centenarians and Offspring" (RADCO), is: centenarian cognitive SuperAgers and some of their offspring have protective factors that confer such resilience or, in some cases, even resistance against cognitive decline and dementia. RADCO assembles an unprecedentedly large sample

of prospectively studied centenarian cognitive SuperAgers (n=495, essentially, centenarians with cognitive function that falls within the norms of septuagenarians) along with offspring (n=600) and offspring spouses (n=120), who, via RADCO cores, undergo careful, comprehensive, and cutting-edge neuropsychological, biomarker, neuroimaging, and neuropathological phenotyping. These data are used by two projects with the overall scientific objective of gauging cognitive resilience in this sample, understanding the underlying protective biology and translating that into therapeutic targets. The Cognitive Resilience and Resistance Phenotypes Project (Project 1) gauges resilience by neuroimaging, plasma AD biomarkers risk and neuropathology, and therefore generates a range of resilience endophenotypes. The Protective Factors and Mechanisms Project (Project 2) is the translation arm of RADCO; it discovers genes, candidate biological pathways and sets of mi-RNA regulators associated with the resilience endophenotypes characterized in Project 1. In-vitro models of AD incorporate cortical neurons, microglial cells, and astrocytes created from centenarian cognitive superager induced pluripotent stem cell (iPSC) lines are used to test the candidate pathways for how they cause resilience against AD.

PUBLIC HEALTH RELEVANCE: Centenarian cognitive SuperAgers have exceptional cognitive function despite extreme exposure to the strongest risk factor for cognitive impairment and Alzheimer's disease, aging. The RADCO Study gauges cognitive resilience among centenarian cognitive SuperAgers and their offspring using cognitive testing, neuroimaging, blood biomarkers, and neuropathology. Translational studies will identify protective factors and underlying mechanisms that confer resilience or in some cases, even resistance against cognitive decline and dementia.

Study to Uncover Pathways to Exceptional Cognitive Resilience in Aging (SUPERAging) U19AG073153

The SUPERAging cooperative agreement (U19AG073153) awarded to Drs. Emily Rogalski, Marsel Mesulam, and Changiz Geula is in its third year of award. This year has seen a change in the locus of the primary award. Dr. Rogalski has transferred from Northwestern University to the University of Chicago. Dr. Mesulam has stepped down as one of the Multi-Principal Investigators (MPI) and remains active on the project as a co-investigator. Dr. Geula remains as an MPI. Both Drs. Geula and Mesulam are still on faculty at Northwestern. The team published findings in the Journal of the American Geriatrics Society in 2023 regarding the medication usage profiles of cognitive SuperAgers compared to age-peers. They reported that the medication profiles of cognitive SuperAgers showed no significant difference compared to cognitively average-for-age older controls in total medications, prescription medications, OTC medications, or in 10 medications/medication categories of interest. In another 2023 publication in Journal of the International Neuropsychological Society, they demonstrated that the episodic memory measure from the NIH Toolbox® is useful for differentiating cognitive SuperAgers from those with average-for-age cognition. These publications are attached to this report.

The abstract for U19AG073153:

DESCRIPTION (provided by applicant): The primary goal is to establish a multicenter SuperAging Consortium to identify behavioral, health, biologic, genetic, environmental, socioeconomic, psychosocial, anatomic and neuropathologic factors associated with SuperAging. These goals will be achieved through an organizational structure with 3 Cores (Administrative/Biostatistics, Clinical/Imaging, and Biospecimen/ Neuropathology) and 2 Research Projects. The Consortium will enroll 500 participants across 4 US Sites located in Illinois, Wisconsin, Michigan and Georgia, and the Canadian Site in Southwest, Ontario, with a focus on the enrollment of Black SuperAgers and Cognitively Average Elderly Controls with similar demographics (Controls). The Administrative/Biostatistics Core will provide governance and fiscal oversight, maintain scientific integrity, and create a centralized biostatistics and database infrastructure to harmonize the goals and activities of the Cores, Sites, and Projects, with each other, with the NIA, and with extramural collaborators. The Clinical/Imaging Core will standardize criteria for the uniform cross-site and multidisciplinary characterization of SuperAgers, streamline recruitment including that of Black participants, enter relevant information in the comprehensive database, support co-enrollment into Project 1, and encourage collaborative ventures aiming to understand the factors that promote SuperAging. The Biospecimen/Neuropathology Core will collect and bank brain tissue and blood products from SuperAging and Control cases, according to optimized procedures. It will render pathological diagnoses, quantitate selected markers of neurodegeneration and neuronal structure, coordinate the analyses of plasma biomarkers for Alzheimer's disease, and make specimens available for collaborative investigations. Project 1 will use state-of-the-art wearable technology to obtain real-time measurements in the course of everyday life to characterize quantitative parameters related to sleep, physical activity, autonomic responsivity, and social engagement to determine whether SuperAgers have relatively preserved and quantitatively determined physiologic and behavioral "complexity" compared to Controls. Project 2 will use transcriptomic, genetic, and protein profiling approaches to test the hypothesis that SuperAgers will demonstrate significant molecular differences in their central and peripheral immune and inflammatory system parameters compared to matched Control and Alzheimer's disease participants. By identifying neurobiologic features that contribute to superior memory performance in old age, outcomes from this Consortium will help isolate factors that promote successful cognitive aging and perhaps also prevent age-related brain diseases such as Alzheimer's disease.

PUBLIC HEALTH RELEVANCE: The proposed Consortium offers optimal organization for the accelerated recruitment of a racially diverse cohort of SuperAgers so that they can be more fully characterized neuropsychologically, neuropathologically, psychophysiologically, and molecularly. The planned activities of the Consortium will help isolate factors important for promoting successful cognitive aging and potentially also for avoiding age-related brain diseases such as Alzheimer's disease.

Follow-on Study of the MEDEX Clinical Trial

Participants in the MEDEX ("Remediating Age-related Cognitive Decline: Mindfulness-based Stress Reduction and Exercise") clinical trial are being followed through a new award (R01AG072694, "Resilience and Brain Health of Older Adults During the COVID-19 Pandemic") to Dr. Eric Lenze (PI of MEDEX; Washington University St. Louis), Dr. Breno Diniz (University of Connecticut School of Medicine), and Dr. Julie Wetherell (University of California San Diego).

The project goals are to elucidate whether exercise and mindfulness can mitigate the effects of stressors from the COVID-19 pandemic on cognitive function and emotional health in later life, including neurobiological measures of risk for Alzheimer's disease. By following the MEDEX participants, repeated sets of clinical, cognitive, molecular, and neuroimaging measures spanning 7.5 years and covering the pre-, during-, and post-pandemic period are being generated.

The abstract for R01AG072694:

DESCRIPTION (provided by applicant): Exercise and mindfulness are believed to be effective stress reduction interventions, but research to date has not been able to assess their benefits while individuals are coping with a major stressor in real time. The COVID-19 pandemic is an unwanted natural experiment in the deleterious effects of stress – especially social isolation (social disconnectedness and loneliness), a stressor particularly strongly associated with the pandemic – on older Americans' cognitive and emotional health and risk for Alzheimer's disease (AD). This project will elucidate whether exercise and mindfulness can mitigate the effects of pandemic stress on cognitive function and emotional health in later life, including neurobiological measures of risk for AD. We will leverage a unique resource: the NIH-funded trial, MEDEX. By leveraging MEDEX and following these participants, who continue to attend monthly booster sessions of their randomized condition remotely during the pandemic, we will have repeated sets of clinical, cognitive, molecular, and neuroimaging measures covering 7.5 years during the pre-, during-, and post-pandemic period. We can examine intervention effects, as well as individual factors such as resilience, on long-term outcomes. Among other innovative aspects of the project, we will analyze effects on two novel peripheral biomarkers: Senescence Associated Secretory Phenotype (SASP), which measures mechanisms of biological aging, and plasma amyloid Aβ42 and Aβ40, which measure AD risk. In the proposed project, (1) during the pandemic, we will use novel methods such as Ecological Momentary Assessment (EMA) to characterize social isolation both objectively (e.g., number of social contacts) and subjectively (e.g., loneliness), and its biological mechanisms on aging (such as elevations in SASP and plasma amyloid); (2) post-pandemic, we will assess downstream effects on cognitive function, emotional well-being, and brain health, including AD risk, using neuropsychological assessments, EMA, and neuroimaging. Outcomes include (Aim 1) changes in cognitive performance and emotional well-being and decline in emotional well-being measured by positive

and negative effect and sleep quality; increases in biological aging and decreasing AB42/40 ratio in the post-pandemic phase, indicating higher risk of AD; and atrophy in hippocampal and prefrontal volume (structural MRI) and reduced global functional connectivity (resting state fMRI). Modifiers of these effects (Aim 2) include exercise and mindfulness; psychological resilience; COVID-19 exposure; medical morbidities; and APOE genotype. Mechanisms of cognitive, emotional, and brain health changes (Aim 3) include amyloid (Aβ40 and Aβ42), SASP, DNA methylation, and cortisol during the pandemic. This project will advance our knowledge of the impact of social isolation and other stressors on older adults, including mechanisms by which these stressors produce deleterious cognitive, emotional, and brain health changes over time, and whether exercise and mindfulness have durable protective effects.

PUBLIC HEALTH RELEVANCE: As referenced above, the COVID-19 pandemic provides an undesired natural measure of the detrimental effects of stress and social isolation on older Americans' cognitive and emotional health and risk for Alzheimer's disease. This project will advance our knowledge of the impact of social isolation and loneliness on older adults, including mechanisms by which these stressors produce negative cognitive, emotional, and brain health changes and how we can prevent those negative effects.

Additional Initiatives Stemming from the Cognitive Aging Summit III

In addition to RFA-AG-21-015 providing support for the two network grants to identify, evaluate, and track cognitive SuperAgers, which was jointly sponsored by the MBRF and the NIA, the NIA launched two additional research initiatives based on knowledge gaps and research opportunities identified from the Cognitive Aging Summit III.

One of the recommendations from the 2017 Summit was to support a longitudinal study of rats that would closely track the animals throughout their lives. NIA's Intramural Research Program (IRP) implemented that recommendation via a longitudinal study in rodents, "Successful Trajectories of Aging: Reserve and Resilience in Rats" (STARRRS). The award was made to Dr. Peter Rapp in the IRP. The study is on track to generate state-of-the-art neuroimaging, along with phenotypic results, non-invasive biological samples, plus other indicators that NIA hopes will yield insight into the mechanisms of healthy neurocognitive aging. The overarching goal of STARRRS is to establish an open resource of longitudinal data from male and female rats, including detailed behavioral characterization and neuroimaging, tissues and other biospecimens, for research on mechanisms of reserve and resilience in aging, and to inform resilience to Alzheimer's disease and related dementias. As of the end of 2023, 440 animals have been enrolled into the project, including animals that now have completed or are nearing completion of the longitudinal study. Brain MRI scans have been collected on almost 100 animals at two time points, along with data from motor activity, memory, attention, olfaction, frailty, and anxiety assessments.

An additional recommendation from the 2017 Summit was to develop operational definitions of constructs such as cognitive reserve, resilience, compensation, etc., that could be used uniformly by researchers. The Summit brought together a multidisciplinary group of investigators with shared interest in research on age-related cognitive decline as well as cognitive reserve and resilience. There was unanimous agreement that a significant barrier to progress in the field was the lack of clear and universally accepted definitions of important concepts related to cognitive reserve and resilience, and that it was imperative to address this deficit. An RFA (RFA-AG-18-024) was released by NIA, and one award was made to Dr. Yaakov Stern and Columbia University Health Sciences for a network grant titled "Collaboratory on Research Definitions for Cognitive Reserve and Resilience" (R24 AG061421).

Through a no-cost extension this past year, Dr. Stern and his co-investigators (Drs. Marilyn Albert, Carol Barnes, Roberto Cabeza, Alvaro Pascual-Leone, and Peter Rapp) were able to continue work on this effort and to hold a fourth workshop. The website for the effort, https://reserveandresilience.com/, contains information for these four workshops, the latest being in early December 2023. The framework for operational definitions of reserve and resilience concepts was published in 2023 in Neurobiology of Aging, along with a Commentary by Dr. Wagster and Dr. King. Both publications are attached to this report. Besides conducting workshops and developing and publishing the framework, this grant allowed for the award of pilot grants to explore and expand the constructs of resilience and reserve in the service of the framework development as well as to establish resources for future exploration. A publication was generated in 2023, resulting in part from one of the pilot awards (see Appendices for full publication): Gray, D. T., et al., Extracellular matrix proteoglycans support aged hippocampus networks: a potential cellular-level mechanism of brain reserve, Neurobiology of Aging, 2023.

The abstract for R24AG061421:

DESCRIPTION (provided by applicant): Research indicates that specific life exposures and genetic factors contribute to some people being more resilient than others, with lower rates of cognitive decline with aging, and reduced risk of developing Alzheimer's disease and related dementias (ADRD). There are likely several complex and highly interactive mechanisms that lead to these individual differences in vulnerability to decline, probably reliant on both structural and functional brain mechanisms. Key concepts often used in research in this area are cognitive reserve, brain reserve and brain maintenance. However, the definitions of these concepts differ across researchers, and the translation from human to animal research is not well developed. Also, their relationship to other invoked concepts such as efficiency, capacity, and compensation are not well explicated. The goal of this project is to work towards achieving state-of-the-art definitions for these concepts to allow researchers to use common nomenclature. In addition, the goal is to validate approaches to help advance research on these approaches that will lead to better maintenance of brain and cognitive health and treatment and/or prevention of ADRD. To that end, we will hold three cross-discipline workshops that will bring together investigators to discuss and come to consensus on these concepts,

create focused workgroups that will examine each of these issues, fund pilot grants designed to further the understanding and research applicability of these concepts, and develop data sharing and information exchange platforms to help guide and promote research in this area.

PUBLIC HEALTH RELEVANCE: To achieve state-of-the-art definitions and research guidelines for key concepts associated with resilience against cognitive aging and Alzheimer's disease related dementias, this project will hold three multidisciplinary workshops, establish focused work groups, create a data sharing and information platform, and support pilot grants designed to further the understanding of these concepts.

APPENDIX

- Journal of the American Geriatrics Society: Medical characterization of cognitive SuperAgers: Investigating the medication profile of SuperAgers
- Journal of the International Neuropsychological Society: NIH Toolbox® Episodic Memory Measure Differentiates Older Adults with Exceptional Memory Capacity from those with Average-for-Age Cognition
- Neurobiology of Aging: A framework for concepts of reserve and resilience in aging
- Neurobiology of Aging: Lost – and Found – in Translation
- Neurobiology of Aging: Extracellular matrix proteoglycans support aged hippocampus networks: a potential cellular-level mechanism of brain reserve

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Medical characterization of cognitive SuperAgers: Investigating the medication profile of SuperAgers

INTRODUCTION

Aging is associated with decline in cognition, with episodic memory changes representing the most common complaint of older adults.[1] SuperAgers are 80+ years with episodic memory capacity at least equal to persons in their 50s to 60s.[2] Their youthful memory phenotype offers a unique model for identifying factors for optimizing healthspan. Initial investigations have identified biologic, genetic, and psychosocial features that distinguish SuperAgers from their average episodic memory peers.[2–4] However, medications have not been characterized.

Medications, both as therapies supporting cognition and as indicators of overall health may contribute to the youthful SuperAging phenotype. Polypharmacy (i.e., use of >5 medications), affects ~40% of US older adults and is associated with increased risk of adverse drug events, falls, and mortality. When considering medication type, opiates, benzodiazepines, and non-benzodiazepine hypnotics are on The American Geriatrics Society (AGS) Beers Criteria list of potentially inappropriate medications (PIMs) for older adults, in part due to their detrimental effects on cognition. Conversely, common medications from antihypertensives to statins to vitamin D have been investigated for possible memory benefits.[5,6]

This study examined whether medication profiles differed between SuperAgers and controls.

METHODS

Community-dwelling participants age 80+ were prospectively enrolled as SuperAgers or cognitively average older controls. Detailed inclusion criteria have been previously reported.[2] Briefly, SuperAgers must perform at or above average normative values for 50–65-year-olds in episodic memory and at least average-for-age normative values in other cognitive domains. Controls were required to perform average-for-age across cognitive domains. The study received institutional review board approval and informed consent was obtained.

Participants reported current medications and supplements, dosage, and duration for each medication/supplement. Staff verified responses. Two physicians independently categorized medications as prescription or OTC; discrepancies were adjudicated by consensus.

Secondary analysis further classified participants as users/non-users of 10 medications/medications classes. Aspirin, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and statins were highlighted given their roles in cardiovascular health. Using the updated AGS Beers Criteria, diuretics, opiates, benzodiazepines, and non-benzodiazepines hypnotics were examined as PIMs. Vitamin D, metformin, and thyroid hormones were included for their potential role in supporting cognition.

Linear regression models were used to analyze differences in the number of medications (prescription, OTC, total medications) used, and logistic regression was used to model binary variables (use versus non-use) for 10 specific medications or medication classes. Race, gender, and age were included as covariates. Uncontrolled *t*-test and Fisher's exact tests were performed for continuous and binary variables respectively. Significance was set at $p = 0.05$.

RESULTS

Table 1 provides demographics and neuropsychological performance for 96 SuperAgers and 46 controls. No significant difference was detected in total, mean prescription, or OTC medication use between SuperAgers and controls in the uncontrolled *t*-test or the linear regression controlling for age, gender, and race (Figure 1). The specified medications/medication use categories also showed no significant difference between groups (Figure 1).

DISCUSSION

The medication profiles of SuperAgers, older adults with exceptional episodic memory, showed no significant difference compared to cognitively average-for-age older controls in total medications, prescription medications, OTC medications, or in 10 medications/medication categories of interest. On average, prescription medications were higher in the current study (SuperAgers: 3.48, controls 3.20) than in larger epidemiologic studies like the Bronx Aging Study (BAS: 2.3) and the Monongahela Valley Independent Elders Survey (MoVIES: 2.0).[7,8] Notably,

Janessa R. Engelmeyer and Alice Kerr contributed equally to the work.

TABLE 1 Demographics and neuropsychological performance.

Demographics	SuperAgers ($n = 96$) [range]	Cognitively normal controls ($n = 46$) [range]
Age (years)	82.3 ± 3.4 [80–101]	84.2 ± 4.7 [79–102]
Education (years)	16.3 ± 2.4 [12–20]	16.7 ± 2.9 [6–20]
Sex, men:women	26:70	17:29
Race, Caucasian:African American	85:11	42:4
Handedness, right:left:ambidextrous	90:4:2	44:2:0
Neuropsychological test performance		
RAVLT delay recall raw score	11.0 ± 1.9	5.7 ± 1.3
Trail making test B raw score	87.9 ± 3.4	106.6 ± 43.3
Category fluency: Animals raw score	21.4 ± 5.2	19.0 ± 5.0
Boston naming test (BNT) 30 item raw score	28.1 ± 2.3	26.9 ± 2.9
Weschler test of adult reading (WTAR) estimated FSIQ (80+)	115.5 ± 8.0	114.4 ± 9.1

Note: Data are shown as means ± standard deviations and [ranges] RAVLT delay: measure of episodic memory with possible scores ranging from 0 to 15. Trail making test B: timed measure of executive function, testing discontinued at 300 s. Category fluency: measure of semantic fluency in which participants list as many items as possible (animals) in 60 s. BNT: measure of object naming with possible scores ranging from 0 to 30. WTAR FSIQ: measure of premorbid intelligence.

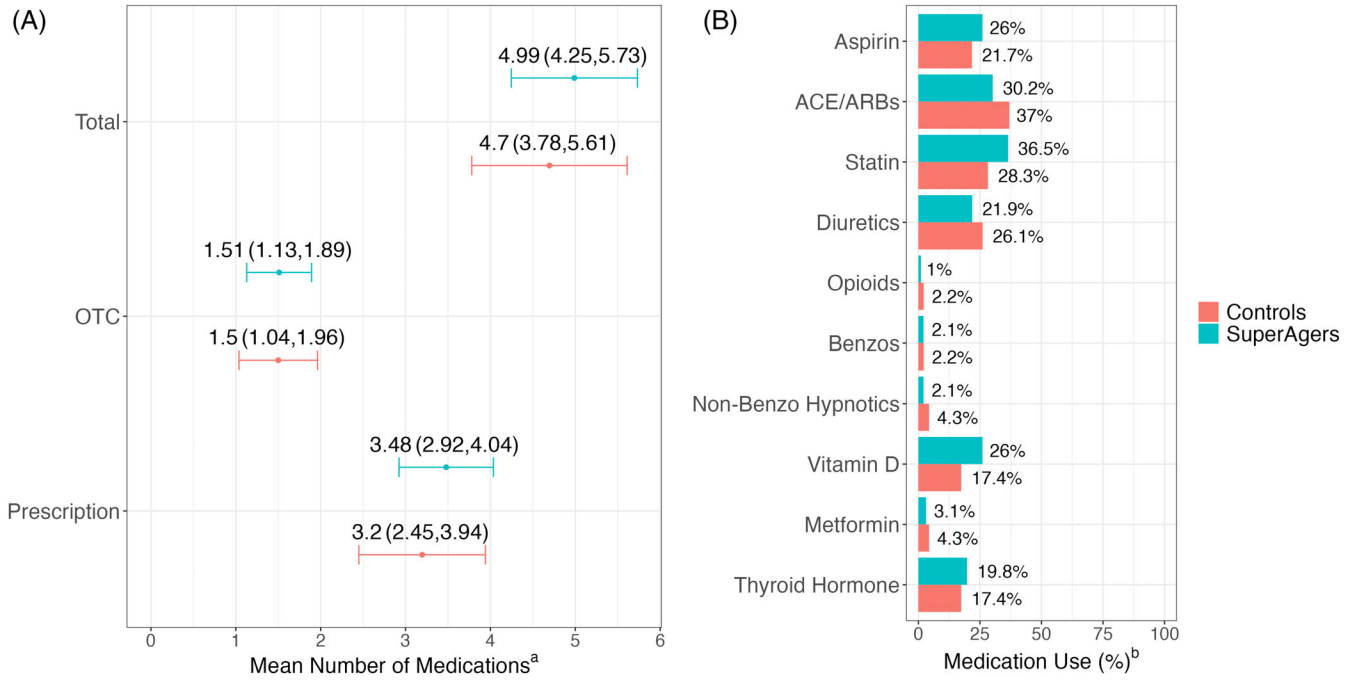

FIGURE 1 Medication use does not differ between SuperAgers and controls. (A) Mean number of medications did not differ between SuperAgers and controls (p values, total: 0.63, OTC: 0.97, prescription: 0.55; or controlled p-values, total: 0.37, OTC: 0.85, prescription: 0.37). (B) Percent of individuals taking a medication did not differ between SuperAgers and controls for p-values range: 0.29–0.82; controlled p-values range: 0.16–97). [a]p-value from a t-test for difference of means. Controlled p-value takes race, gender, and age into consideration using a linear regression analysis. [b]p-value from a Fisher's exact test. Controlled p-value takes race, gender, and age into consideration using a logistic regression analysis. ACE/ARBs, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; benzos, benzodiazepines; OTC, over the counter.

these studies were completed over 20 years prior with younger participants (average age: 79.2, 73.1 years, respectively). Higher use in the current study likely reflects temporal changes rather than intrinsic medical differences, given that prescription use increases over the life span and in recent decades.[9]

Use of potentially inappropriate medications tended to be lower in this study than National Social Life, Health, and Aging Project (NSHAP) cohort, a representative sample of adults aged 57–85 at enrollment.[10] Statins were the most commonly used medications for both SuperAgers (36.5%) and controls (28.3%), while the NSHAP was 46.2%. Similarly, the NSHAP participants reported higher aspirin use (40.2%) compared to SuperAgers (26.0%) and controls (21.7%). Definitive conclusions cannot be drawn without statistical comparison; however, higher use of these medications in larger, representative samples of older adults relative to this study raises the possibility our controls may not represent typical older adult medication use.

In summary, while SuperAgers differ in memory performance from controls, their medication use—total, prescription, and pre-specified subclasses of medication use—did not differ. Thus, distinctive medication profiles cannot fully account for memory performance differences between SuperAgers and cognitively average older adults. However, our previous findings point to slower brain atrophy and psychosocial factors, as potential contributors to youthful memory performance.[2–4]

AUTHOR CONTRIBUTIONS

Janessa R. Engelmeyer contributed to data acquisition, analysis, and drafted the manuscript. Alice Kerr contributed to data analysis, interpretation and drafted the manuscript. Beth A. Makowski-Woidan contributed to data acquisition and critical revision of the manuscript. Nathan P. Gill and Hui Zhang contributed to data analysis, interpretation, and critical revision of the manuscript. Lee Lindquist contributed to analysis, interpretation, and critical revision of the manuscript. M.-Marsel Mesulam, Sandra Weintraub, and Emily J. Rogalski contributed to the study conception and design, data acquisition, and critical revision. All authors gave final approval and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

Emily J. Rogalski, M.-Marsel Mesulam, Hui Zhang, Nathan P. Gill, Lee Lindquist, and Sandra Weintraub report NIH funding. Emily J. Rogalski, M.-Marsel Mesulam, and Sandra Weintraub report receiving honoraria.

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The sponsor was not involved in the design, methods, subject recruitment, data collection, analysis, or preparation of the manuscript.

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Janessa R. Engelmeyer BA[1]
Alice Kerr MD[2]
Beth A. Makowski-Woidan BA[1]
Nathan P. Gill PhD[3]
M.-Marsel Mesulam MD[1,4]
Sandra Weintraub PhD[1,5]
Hui Zhang PhD[3]
Lee Lindquist MD, MPH, MBA[6]
Emily J. Rogalski PhD[1,5]

[1]*Mesualm Center for Cognitive Neurology and Alzheimer's Disease, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[2]*Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[3]*Division of Biostatistics, Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[4]*Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[5]*Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[6]*Division of General Internal Medicine and Geriatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*

Correspondence
Janessa R. Engelmeyer, Mesulam Center for Cognitive Neurology and Alzhiemer's Disease, Northwestern University Feinberg School of Medicine, 300 East Superior Street, Tarry 8, Chicago, IL 60611, USA.
Email: jrengelmeyer@gmail.com

ORCID

Janessa R. Engelmeyer https://orcid.org/0000-0002-3973-6256
Lee Lindquist https://orcid.org/0000-0002-4290-5081

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BRIEF COMMUNICATION

NIH Toolbox® Episodic Memory Measure Differentiates Older Adults with Exceptional Memory Capacity from those with Average-for-Age Cognition

Tatiana Karpouzian-Rogers[1,2,*], Beth Makowski-Woidan[2], Alan Kuang[3], Hui Zhang[3], Angela Fought[4], Janessa Engelmeyer[2], M.-Marsel Mesulam[1,5], Sandra Weintraub[1,2] and Emily Rogalski[1,2]

[1]Mesulam Center for Cognitive Neurology and Alzheimer's Disease, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
[2]Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
[3]Division of Biostatistics, Department of Preventative Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
[4]Department of Biostatistics and Informatic, Colorado School of Public Health, University of Colorado-Denver Anschutz Medical Campus, Aurora, CO
[5]Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

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Abstract

Objective: Older adults with exceptional memory function, designated "SuperAgers," include individuals over age 80, with episodic memory at least as good as individuals ages 50s–60s. The Northwestern University SuperAging cohort is defined by performance on an established test of verbal memory. The purpose of this study was to determine if superior verbal memory extends to nonverbal memory in SuperAgers by examining differences in the National Institutes of Health Toolbox® (NIHTB) between older adults with exceptional memory and those with average-for-age cognition. **Method:** SuperAgers ($n = 46$) and cognitively average-for-age older adults ($n = 31$) completed a comprehensive neuropsychological battery and the NIHTB Cognition module. Multiple linear regressions were used to examine differences on subtests between groups. **Results:** There was a significant effect of group on the Picture Sequence Memory score, ($p = .007$), such that SuperAgers had higher scores than cognitively average-for-age older adults. There were no other group effects across other non-episodic memory NIHTB Cognition measures. **Conclusions:** Findings from this study demonstrated stronger performance on the memory measure of the NIHTB in SuperAgers compared to cognitively average-for-age older adults demonstrating superior memory in not only verbal but also nonverbal episodic memory in this group. Additionally, this study adds to the literature validating the NIHTB in older adults, particularly in a novel population of adults over age 80 with exceptional memory.

Keywords: "SuperAgers", normal aging, NIH Toolbox, memory, cognition, dementia

INTRODUCTION

Decline in memory functions is often accepted as part of "normal" aging, with mild changes beginning in mid-life and more accelerated changes occurring over the age of 60 (Nyberg et al., 2012). However, at the Northwestern Mesulam Center for Cognitive Neurology and Alzheimer's disease, we have identified a group of individuals that we designated "SuperAgers," who are over age 80 and able to maintain superior memory performance compared to their same age peers and at a level that is at least "average" for 50- and 60-year-olds (Rogalski et al., 2013). Longitudinal follow-up of these individuals suggests that superior memory performance can be maintained over time, providing additional support for their resistance to the typical age-related decline (Gefen et al, 2014; Rogalski et al., 2019). With respect to psychological factors, SuperAgers report greater levels of social relationships compared to cognitively average-for-age peers (Cook Maher et al., 2017). Neuroimaging studies have demonstrated greater cortical integrity and slowed rates of atrophy compared to cognitively average age-matched peers and thicker anterior cingulate cortex compared to

*Correspondence and reprint requests to: Tatiana Karpouzian-Rogers, PhD, 320 E. Superior St., Chicago, IL 60611, USA. E-mail: t-karpouzian@northwestern.edu

50-–65-year-olds (Harrison et al., 2012; Cook et al., 2017). Further, post-mortem studies suggest a lower frequency of Alzheimer neuropathology and higher density of von Economo neurons in the anterior cingulate compared to cognitively average older adults and individuals with amnestic mild cognitive impairment (Gefen et al., 2015).

The operationalization of memory capacity in SuperAgers was defined on the basis of scores on the Rey Auditory Verbal Learning Test (RAVLT), a difficult 15-item list-learning test of verbal episodic memory, which is widely used and has good psychometric properties. However, performance on tests of other episodic memory measures, including memory tests that place less emphasis on verbal abilities, has not been systematically investigated in this population. A recent research tool that was designed to measure cognitive functions in adults is the National Institutes of Health Toolbox® for Assessment of Neurological and Behavioral Function (NIHTB; Gershon et al., 2013; Weintraub et al., 2014). Traditionally, the evaluation of cognitive abilities in older adults has included either brief cognitive screening measures or lengthy neuropsychological batteries that often require clinical expertise and these batteries frequently differ across studies, making direct comparisons difficult to conduct. The NIHTB is a computerized suite of tests that measure cognitive, emotional, motor and sensory domains in individuals aged 3–85, and was designed to be used across a variety of settings, particularly in longitudinal research studies so that findings across studies could be conveniently compared. The Cognition Module includes a test of episodic memory, the Picture Sequence Memory test, that relies less heavily on verbal abilities, requiring participants to recall sequences of pictured actors and actions in the order they were originally learned over several trials.

The present study examined differences across all subtests of the Cognition module of the NIHTB between older adults with exceptional memory and those who are cognitively average-for-age. Our particular focus was to determine if the NIHTB episodic memory test specifically, which is less reliant on verbal abilities in comparison to our gold-standard of memory capacity, would be sensitive to differences between SuperAgers and "normal" agers. This is important as it would extend the contexts in which SuperAgers display superior episodic memory performance and opens the possibility of using the NIHTB as an efficient tool for future identification of SuperAgers. This study is also the first characterization of NIHTB Cognition module in an established cohort of older adults with exceptional memory. Given that SuperAgers display superior memory capacity, we hypothesized that the SuperAger group would demonstrate greater performance on the episodic memory test of the NIHTB.

METHODS

Participants

Participants 80 years or older were recruited through the Mesulam Center and Northwestern's Alzheimer's Disease Research Center Clinical Core, community lectures, and/or word of mouth. SuperAgers were referred on the basis of high memory scores and the absence of impairment in any other cognitive domain but were not necessarily superior in non-memory domains. Inclusion criteria for SuperAgers included: (1) score at or above the average level for 50–65-year-olds (equivalent to the Superior range for their own age) on the delayed recall condition of the (RAVLT; Schmidt, 1996), a 15-word list-learning memory test; and (2) performance within one standard deviation of the average range for their age on nonmemory measures including the Trail Making Test Part-B, Category Fluency Test, and 30-item Boston Naming Test according to published normative data (Heaton, 2004, Randolph, 1998, Mack et al., 1992). Inclusion criteria for Cognitively Average-for-Age Older Adults included: performance within the average-for-age normative range on the RAVLT and on all non-memory tests administered in the study. Full scale IQ was measured using the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III). Additional inclusion criteria for both groups were that all participants maintained their cognitive status (as measured by neuropsychological battery described above) from their visit to the time the NIH Toolbox® was administered to maintain the integrity of our SuperAger sample. The administration of the NIHTB and collection of the neuropsychological battery occurred no more than three months apart. Additionally, all participants were required to have preserved activities of daily living. Participants with significant neurologic or psychiatric illnesses were excluded. All participants provided written informed consent. The Institutional Review Board at Northwestern University approved all study procedures. Research was completed in accordance with the Helsinki Declaration.

Study Measures

As described in previous studies (Gefen et al., 2014), all participants underwent a neuropsychological battery, including measures of attention, executive functions, language, and episodic memory. Participants completed the Cognition module of the NIH Toolbox® as part of the biyearly standardized battery. The Cognition Battery consists of tests assessing Executive Function and Attention (Dimensional Change Card Sort Test and Flanker Inhibitory Control and Attention Test), Episodic Memory (Picture Sequence Memory Test), Language (Oral Reading Recognition Test and Picture Vocabulary Test), Processing Speed (Pattern Comparison Processing Speed Test), and Working Memory (List Sorting Working Memory Test) (Weintraub et al., 2014). In addition to individual test scores, Cognitive Function, Fluid Cognition, and Crystallized Cognition composite scores are computed. In the Picture Sequence Memory Test, participants are shown a series of pictures depicting a sequence of events, for example, playing in the park. Then, the pictures are assembled in the center of the screen and participants are asked to reproduce the spatial placement of the previously demonstrated sequence of pictures. For additional details on these modules, refer to the original publications (Weintraub et al., 2013; Gershon et al., 2010; Gershon et al., 2013) and the NIHTB website (nihtoolbox.org).

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Table 1. *Study sample characteristics and NIHTB subtest scores*

	SuperAgers ($n = 46$)	Cognitively average-for-age 80+ year-olds ($n = 31$)	Test statistic (t or χ^2)
Demographics and estimated IQ			
Age, mean (SD)	84.2 (3.3)	84.0 (3.9)	.3
Sex, M:F	10:21	16:30	.1
Race, CA:AA	43:3	24:7	.3
Years of education, mean (SD)	17.2 (2.1)	16.5 (2.0)	1.3
WAIS-FSIQ, mean (SD)	133.0 (12.2)	118.7 (15.2)	4.5***
Performance on Standardized Neuropsychological Measures used for Study Inclusion			
RAVLT Delay Raw, mean (SD)	11.0 (1.8)	5.2 (1.4)	1.3***
BNT-30 Raw, mean (SD)[a]	28.2 (1.6)	26.3 (2.8)	3.5**
Animal Fluency Raw, mean (SD)[b]	22.7 (4.4)	19.8 (5.3)	2.6**
Trails B Raw (s), mean (SD)	78.9 (28.3)	104.0 (42.9)	2.9**
NIH toolbox performance			
Oral reading recognition (Language), mean (SD)	7.4 (1.3)	6.2 (2.1)	.03
Picture vocabulary (Language), Mean (SD)	7.8 (1.7)	6.9 (2.0)	.1
Flanker inhibitory control (Executive Attention), mean (SD)	7.4 (.6)	7.2 (.9)	.5
Dimensional Card Sort, (Executive Switching), mean (SD)	7.5 (.7)	7.4 (.8)	.5
Pattern comparison (Processing Speed), mean (SD)	35.5 (9.4)	33.5 (8.0)	.0
List sorting (Working Memory), mean (SD)	15.5 (2.4)	14.6 (3.1)	.1
Picture sequence memory (Episodic Memory), mean (SD)	441.2 (65.8)	388.0 (58.9)	7.7**

*$p < .05$, **$p < .01$, ***$p < .001$
SD = standard deviation; M = male; F = female; CA = Caucasian; AA = African American.
*Note two participants (1 control, 1 SuperAger) had low Boston Naming Test (BNT) scores at the time of NITB but met qualifying criteria at their initial visit. Four participants (3 Controls, 1 SuperAger) had consistently low BNT scores, for one English was a second language and may have contributed to lower scores. These participants were retained in all analysis as there were no other objective or subjective reports of difficulty with language.

Statistical Analyses

Differences in participant demographics were assessed using two-sample *t*-tests. NIH Toolbox® scores were summarized using frequencies and percentages for categorical variables or mean and standard deviation for continuous variables. Histograms and scattered plots of each NIH Toolbox® measure were examined to explore the shape of distributions and identify potential outliers. For the Cognition Module, computed scores were calculated for Flanker, Dimensional Change Card Sort, Pattern Comparison, and Picture Sequence Memory subtests, theta scores were calculated for Reading and Vocabulary, and raw scores were used for List Sorting. For details regarding computation of theta and computed scores, refer to NIHTB Scoring and Interpretation Guide (http://www.healthmeasures.net/images/nihtoolbox/Training-Admin-Scoring_Manuals/NIH_Toolbox_Scoring_and_Interpretation_Manual_9-27-12.pdf). Composite scores were calculated by averaging the normalized scores of each measure, and then deriving scale scores based on this new distribution. For each NIH Toolbox® measure, multiple linear regressions were used to examine differences between groups. Covariate adjustments included Wechsler Adult Intelligence Scale -Full Scale Intelligence Quotient (WAIS-FSIQ), sex, age, and education. Linear regression model fit was assessed using measures of collinearity and non-linearity, including residuals *versus* fits plots, histograms, Q-Q plots of residuals, and Dfbeta statistics. Adjusted R2 values were used to summarize variability explained in the linear models. All analyses were conducted in R 3.5.3 software.

RESULTS

Groups did not differ with respect to age, race, years of education, or sex (*ps* > .05) (Table 1). SuperAgers had a higher WAIS-FSIQ than cognitively average-for-age older adults ($p < .001$). Across all linear models, r-squared values ranged from .03–.34. Collinearity was not a concern, with pairwise correlations ranging from 0 to .56 for model covariates. Multicollinearity was not a concern, with variance inflation factor ranging from 1.03 to 1.79. Dfbeta statistics indicated there are some observations of influences. In order to improve linearity for measures that were positively skewed, scores were log-transformed, which included scores on the Picture Sequence Memory test.

Within the Cognition Module, there was an effect of group on Picture Sequence Memory scores (F (1,63) = 7.7, $p = .007$, $\beta = .10$), such that the SuperAger group had higher scores than the Cognitively Average-for-Age Older Adults (Figure 1). The effects of sex, age, education level, and FSIQ were not significant in this model. There were no other

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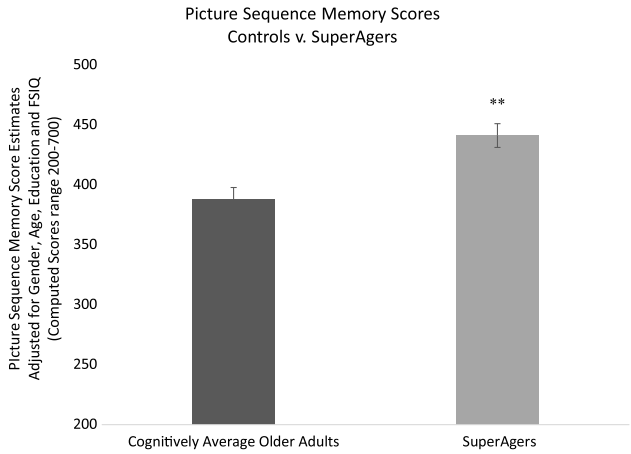

Fig.1. SuperAgers perform significantly better than cognitively average-for-age 80+ year-olds on the NIH Toolbox® Picture Sequence Memory. $^{**}p < .01$

effects of group across all other NIHTB Cognition tests of non-memory domains or on Composite Scores (all *p*s > .05).

DISCUSSION

This study sought to extend the superiority of episodic memory compared with other cognitive domains in the Northwestern University SuperAging cohort by comparing SuperAgers with cognitively average-for-age older adults on the tests of the NIHTB Cognition Battery. Findings of this study demonstrated greater performance on a test reliant on nonverbal episodic memory, the Picture Sequence Memory Test, in the SuperAging group compared to cognitively average-for-age older adults. Performance across all other measures of cognition on the NIHTB were comparable between groups. These findings confirm the exceptional episodic memory in SuperAgers.

The criteria for inclusion in the Northwestern University SuperAging research program involve completion of neuropsychological measures examining multiple aspects of cognition, with particular emphasis on memory abilities. SuperAging status requires performance at or above the average level of 50–65-year-olds on the RAVLT, a well-established measure of verbal episodic memory shown to be sensitive to early changes in memory and structural brain changes in Alzheimer's disease (e.g., Estévez-González et al., 2003). Longitudinal studies of SuperAgers have demonstrated that superior memory performance tends to be stable, suggesting that exceptional memory capacity is not necessarily a function of superior premorbid cognitive abilities, but rather a resistance to age-related cognitive changes (Gefen et al., 2014; Rogalski et al., 2019). The finding that performance on the NIHTB Picture Sequence Memory, a measure of episodic memory that places less emphasis on verbal memory abilities, also differentiates the SuperAging group and cognitively average-for-age older adults is further confirmation of the memory superiority in SuperAgers. This suggests that superior memory capacity in SuperAgers may not be specific to the list learning of the RAVLT, but is more general to episodic memory. Additionally, scores on all other NIHTB measures were similar between groups, which mirrors our criteria that SuperAgers may score in at least the average range on all other measures of cognition, including object naming, semantic fluency, and executive attention. Although it is unclear why there were no differences at the group level across other NIHTB subtests, it is possible there may be nuanced profiles at the individual level; this is similar to what was observed in recent work from the SuperAging Research Program, which demonstrated significant intragroup variability on multiple cognitive domains (Maher et al., 2021). Additional explanations include differences in the specific domains assessed by our neuropsychological measures *versus* the NIHTB (i.e. verbal fluency), as well as differences in tests used in this study compared to the neuropsychological tests used to validate the NIHTB (Weintraub et al., 2013).

The NIHTB has been validated in older adults without cognitive impairment and has also been investigated in older adults with varying degrees of cognitive impairment. In particular, one study examined the psychometric properties of the NIHTB cognition module in cognitively intact older adults and found acceptable test-retest reliability over a one-year period, as well as a relationship between NIHTB Fluid Composite and cerebral volumes, and a strong correlation between Fluid and Crystallized Composites with their respective gold standard composites (Scott et al., 2019). In a study of older adults with subjective decline, mild cognitive impairment, or mild dementia, performance on the NIHTB Cognition module was consistent with performance on traditional neuropsychological tests and had greater discriminative ability when supplemented with RAVLT delayed recall performance (Hackett et al., 2018). Further, neuroimaging studies have demonstrated relationships between NIHTB performance and hippocampal volume and tau deposition in older adults (O'Shea et al. 2016; Snitz et al., 2020). One important limitation is that the sample was a predominantly white, well-educated group, and therefore replication with a more diverse sample is needed. The present study is one of the first, to our knowledge, to examine performance in the NIHTB in an established cohort of adults over age 80 with exceptional memory and adds to the utility of using the NIHTB to measure cognitive functioning in the oldest of old age groups.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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Commentary

A framework for concepts of reserve and resilience in aging

Yaakov Stern[a,*], Marilyn Albert[b], Carol A Barnes[c], Roberto Cabeza[d], Alvaro Pascual-Leone[e], Peter R. Rapp[f]

[a] Cognitive Neuroscience Division, Department of Neurology, Columbia University Vagelos College of Physicians and Surgeons, New York, NY, USA
[b] Departments of Psychiatry and Neurology, John Hopkins University, Baltimore, MD, USA
[c] Departments of Psychology, Neurology and Neuroscience, and Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ, USA
[d] Center for Cognitive Neuroscience, Department of Psychology and Neuroscience, Duke University, Durham, NC, USA
[e] Department of Neurology, Harvard Medical School, Boston, MA, USA
[f] Laboratory of Behavioral Neuroscience, Neurocognitive Aging Section, National Institute on Aging, Baltimore, MD, USA

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ABSTRACT

The study of factors, across species, that allow some individuals to age more successfully than others has important implications for individual wellbeing as well as health education, policy and intervention. Design of studies and communication across investigators in this area has been hampered by a diversity of terminology. The Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia was funded by the National Institute on Aging and established in 2019 as a 3-year process of developing consensus definitions and research guidelines. The proposed Framework is based on an iterative process including 3 annual Workshops, focused workgroups, and input from numerous international investigators. It suggests the overarching term: resilience, and presents operational definitions for 3 concepts: cognitive reserve, brain maintenance, and brain reserve. Twelve pilot studies that integrate these definitions are presented. The use of a common vocabulary and operational definitions will facilitate even greater progress in understanding the factors that are associated with successful aging.

1. Introduction

The study of factors that allow some individuals to age more successfully than others, including for example genetics and life exposures, has important implications for individual wellbeing as well as health education, policy and intervention. Moreover, identifying factors that are relevant across species (i.e., humans and nonhumans) is fundamentally necessary to facilitate studies of the neurobiological underpinnings of such factors.

In this context, overarching concepts like reserve and resilience are often invoked for capturing differential susceptibility to brain aging and disease. However, design of studies and communication across investigators in this area has been hampered by a diversity of terminology. Several groups have published proposed nomenclature and operational definitions for concepts including resilience, cognitive reserve (CR), brain reserve (BR), brain maintenance (BM), compensation, scaffolding, resistance, and resilience. Across these papers there are often disparate definitions for the same term. In addition, most of these papers focus on human studies, so the definitions and nomenclature are not optimally suitable for nonhuman studies.

The Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia was funded by the National Institute on Aging of the National Institutes of Health in the USA and established in 2019 as a 3-year process of developing consensus definitions and research guidelines for CR and related concepts. The present document is the result of an iterative process including 3 large annual Workshops, input from focused workgroups, and the extensive participation and consultation of over 40 selected, international expert investigators who utilize multiple research approaches and study both humans and nonhumans. Here we present a framework that includes definitions for 3 concepts, CR, BM, and BR, along with suggested operational definitions to help guide the design of research investigating these concepts. We also include resilience as an overarching term that subsumes all of the concepts presented.

Our aim is to present a well-defined set of operational definitions in order to encourage, advance, and develop research on

Abbreviations: CR, Cognitive reserve; BM, Brain maintenance; BR, Brain reserve.

* Corresponding author at: Columbia University Vagelos College of Physicians and Surgeons, 630 W 168th St, P&S Box 16, New York, NY 10032, USA, Phone: 212-342-1350.
E-mail address: ys11@columbia.edu (Y. Stern).

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these concepts. At the same time, we want to encourage investigators who have different views or use a given concept differently to note how their definitions relate or differ with one of those described here. Similarly, this framework provides a basis for describing how the operational definition of another concept differs from those suggested here.

Our intention is not to limit the creativity or ingenuity of investigators, or to claim that the framework presents the only way to investigate these important concepts. We hope to encourage research that provides either evidence-based support for these concepts or that presents data that cannot be accommodated by the proposed operational definitions of these concepts. We also hope that referring to this framework will facilitate collaboration and comparison of findings across studies and species.

The Collaboratory also sponsored 12 studies that were intended to implement the suggested research guidelines and thus provide experimental examples of their operational utility. This disparate set of studies incorporates humans and nonhumans, as well as multiple approaches including epidemiologic, neuroimaging, and interventions. We include in the supplementary material descriptions of the pilot projects as wells as a table that summarizes the projects and how they incorporate the framework presented here. These provide useful real-world examples that illustrate how study designs can incorporate the suggested framework.

Our hope for this framework is that the use of a common vocabulary and operational definitions will facilitate even greater progress in understanding the factors that are associated with successful aging.

2. Resilience

The term resilience has been used in many contexts. Here we consider it a general term that subsumes any concept that relates to the capacity of the brain to maintain cognition and function with aging and disease. There can be substantial variability in the mechanisms underlying resilience. Here, we present 3, CR, BM, and BR.

3. CR

3.1. Definition

CR is a property of the brain that allows for cognitive performance that is better than expected given the degree of life-course related brain changes and brain injury or disease:

- Property of the brain refers to multiple potential mechanisms including molecular, cellular and network levels. The working hypothesis is that these mechanisms help cope with or compensate for brain changes and the consequences of brain injury or disease.
- These mechanisms can be characterized via biological or cognitive-experimental approaches.
- Better than expected cognitive performance refers to differences ideally measured longitudinally.

CR can be influenced by multiple genetic and environmental factors, operating at various points or continuously across the lifespan.

3.2. Operational definition: general considerations

Research aimed at further elucidating CR requires the inclusion of 3 components:

1. Measures of life course-related brain changes, insults, disease, or risk factors that theoretically impact cognitive outcomes,
2. Measures of associated change in cognition, and
3. A variable that influences the relationship between 1 and 2.

Ideally, the aim is to demonstrate that any proposed CR measure (e.g., a sociocultural or functional brain measure) moderates the relationship between 1 and 2. For example, in an analysis where change in brain atrophy/pathology measures (component 1) predict change in cognition (component 2), and includes education as a hypothesized CR proxy (component 3), there is a statistical interaction between brain measures and education, such that level of education significantly moderates the association of brain measures with cognitive change.

Even without evidence for moderation, it can also be sufficient to demonstrate that a hypothesized CR proxy or measure is associated with cognitive performance over and above (e.g., after adjusting for) the effects of brain change, pathology, or insult. For example, in a multiple regression analysis of change in cognition that includes brain atrophy/pathology measures and a hypothesized CR proxy, the proxy should account for variance in cognitive performance. In this analysis, the CR proxy simply adds predictive information (a protective factor), a weaker form of CR evidence than moderation.

All 3 components are needed when investigating CR. For example:

Demonstrating that expression of higher connectivity within a specific resting BOLD network is associated with slower cognitive decline is not sufficient to conclude that expression of this network reflects CR. To make a claim about CR it must also include measures of age-related brain change, insult or disease that theoretically impact cognitive outcomes.

Similarly, a relationship between a particular genotype and rate of cognitive decline would not be sufficient to conclude that this genotype is associated with CR. It would be important to demonstrate that the genotype's relationship to reduced rates of cognitive decline is expressed through moderation of age-related brain change or reduction of the expected impact on cognitive performance of a given brain insult or disease.

3.3. Specification of the 3 components needed to elucidate CR

3.3.1. Measures of life course-related brain developmental changes, injury, or disease that theoretically impact cognitive outcomes

This could consist, for example, of measures of anatomic changes such as loss of brain volume or white matter tract integrity, or onset and progression of disease pathology such as biomarkers of neurodegenerative disease.

These changes could be more extensively specified. Measures/mechanisms underlying aging that impact cognitive outcomes could include change in structure or function of synapses, oxidative damage/stress, impaired stress response signaling, Ca2+ dyshomeostasis and/or dysregulation, mitochondrial function, impaired waste disposal, inflammation, epigenetics, stem cell depletion, and altered neuronal activity/connectivity.

It is likely that unmeasured or unknown brain or pathologic changes contribute to inter-individual variance in the cognitive outcomes. Their eventual inclusion would increase the precision of elucidating CR.

3.3.2. Measures of cognition

This term encompasses measures of cognition and day-to-day function that change with aging and disease. When possible, it would be useful to adopt cognitive tests that show changes with age or brain disease, and that can be used across species. In this case, it is important to be mindful that formal operational similarity between human and nonhuman tasks is not sufficient, or even necessary; the tasks need to tap similar underlying neural systems.

3.3.3. CR proxy/mechanism:*a hypothesized variable that influences the relationship between 1 and 2*

As the definition of CR states, these mechanisms can be characterized via biological or cognitive experimental approaches.

Proxies for CR in human studies have included features associated with both endowment and experience, including early age IQ, cognitively stimulating exposures across the age span, education, occupational exposures, leisure activity, social networks, or other exposures, hypothesized or to be discovered, that might impart CR. Similar proxies such as behavioral training, physical exercise, environmental enrichment, social housing, or diet are applicable to nonhuman studies.

In addition, the nature of the CR proxy or mechanism that influences the relationship between component 1 and 2 can be explored. For example, investigators might explore whether differential expression of a specific functional network is associated the degree of sustained cognitive function in the face of age-related brain changes that impact cognition. More generally, mechanisms underlying CR could be specified at the molecular, cellular or network levels.

3.4. Example of studies of CR

In studies of CR, longitudinal designs optimally address the 3 features underlying the concept of CR. However, rich information can be gained from cross-sectional studies including discovering variables that appear to be critical for CR, establishing preliminary observations, providing insight into neurobiological mechanisms and developing research or conceptual approaches.

3.4.1. Longitudinal study incorporating measures of brain and cognitive change

In a longitudinal study, one could explore whether some life exposure conceptually linked to CR moderates the relationship between change in brain status (e.g., volume, white matter tract integrity, white matter hyperintensity burden) and change in cognition. For example, one could establish a relationship between age-related changes in cortical thickness/surface area, brain volume, and white matter tract integrity with changes in cognition. The potential moderation by education of this relationship could then be explored. Such moderation would provide support for the idea that higher education is associated with CR.

Some longitudinal studies may have no direct measures of brain change. Analyses that assume parity across all followed individuals or incorporate risk factors for brain changes could suggest hypotheses and guide subsequent studies.

3.4.2. Neural implementation of CR

Although variables such as IQ, education, occupational attainment etc. can be associated with CR as described in 4.1, that is, moderating between measures that theoretically impact cognitive outcomes (component 1) and measures of associated change in cognition (component 2), more insight into the mechanisms underlying CR might be obtained from studies that directly examine neural mechanisms. In both human and nonhuman studies, imaging techniques including functional MRI (fMRI), spectroscopy, and EEG are uniquely suited for longitudinal measurements, providing in-depth assessments of brain structure, neural activity, and the chemistry in the aging brain. CSF, plasma/serum, and extracellular vesicle biology in blood are advancing rapidly and may provide a translatable fluid biopsy for relevant brain changes in this context.

Thus, one goal might be to identify functional networks or circuits, whose differential expression moderates the relationship between age-related brain changes that impact cognitive outcomes and the associated change in cognition. For example, longitudinal studies of aging or neurodegenerative disease can investigate how the relationship between changes in structure/function and cognition/clinical status can be moderated by proposed reserve-related networks. It would be of interest to determine whether differential expression of this network is related to life exposures such as education or occupational experience. This would create a relationship between a proxy for CR and a potential brain mechanism underlying that proxy.

3.4.3. Intervention studies and natural experiments

Intervention studies can most directly test whether some exposure or mechanism underlies CR by examining whether the intervention moderates the effect of age-related brain changes on cognitive outcomes. These studies can help explore mechanisms underlying CR.

Similarly, controlled perturbations such as transcranial magnetic or direct current stimulation could model brain insult, stressor or disease. Alternately, they could be used to modulate activity in networks/circuits associated with CR, and by suppressing it or facilitating it, gain causal and mechanistic insights, and even potentially explore therapeutic interventions.

Sometimes, environmental changes can be used as natural experiments. A natural experiment is a situation when some change occurs in the environment that is not under experimental control and approximates random assignment. An example of such a natural experiment is changes to compulsory schooling laws. Conversely, animal models that feature increased individual differences in cognitive aging, under conditions of tightly controlled life-course exposures, can test for inherent genetic and biological moderators or mediators of CR. Quasi-experimental twin design is closest to this experimental design in humans. This design can utilize co-twins with different levels of exposures such as educational or occupational attainment.

4. BM

4.1. Definition

BM refers to the relative absence of changes in neural resources or neuropathologic change over time as a determinant of preserved cognition in older age.

BM can be influenced by multiple genetic and environmental factors, operating at various points across the lifespan.

4.2. Operational definition

BM is influenced by factors (genes, sex, early life influence or differential experiences) that slow or prevent brain changes associated with aging and disease. The emphasis centers on change over time. Thus, BM may be operationalized as minimal changes in brain markers of aging or disease associated with preservation of cognitive function.

Research aimed at further elucidating BM requires the inclusion of 3 components.

1. Measures of age-related brain changes, injury or disease that theoretically impact cognitive outcomes,
2. Measures of change in cognition.

Demonstrating a link between less change in 1 and less change in 2 would be evidence of BM.

To investigate potential mechanisms of individual differences in BM one could examine:

1. A hypothetical variable that influences 1.

This variable can encompass many of the same exposures potentially associated with CR. However, their impact on BM in this context would be specific to maintaining the structural and functional integrity of the brain.

4.3. Example studies of BM

BM is optimally ascertained in longitudinal designs. A single time point measurement cannot definitively differentiate people who have maintained their brain from those who did not but started at a higher baseline level. In both human and nonhuman studies this issue can be addressed to some degree by determining what level of brain status is expected for a particular age, or considering a given brain measure relative to the distribution seen in younger subjects. However, longitudinal designs are preferable to examine factors underlying interindividual differences in the change in neural resources that are in turn associated with differences in cognitive outcomes.

4.3.1. Longitudinal study of BM

A general approach to studying BM would be to examine longitudinally whether individual differences in the rate of age- or disease-related brain anomalies accumulated over time are related to individual differences in the rate of cognitive change.

4.3.2. Exposures related to BM

An extension of study 3.1 would be to assess potential proxies or mechanisms (e.g., genetic, lifestyle, neural) that are associated with these different trajectories of BM/change.

In summary, BM and CR are complementary concepts. BM accounts for individual differences in cognitive trajectories that are associated with differences in rate of brain change. In contrast, CR addresses individual differences in cognitive trajectories controlling for changes in neural resources or neuropathology.

5. BR

5.1. Definition

BR has been used to reflect the neurobiological status of the brain (numbers of neurons, synapses, etc.) at any point in time. BR does not involve active adaptation of functional cognitive processes in the presence of injury or disease as does CR.

5.2. Operational definition and example studies

Research aimed at further elucidating BR requires the inclusion of 2 components:

1. Measures of brain features that theoretically are associated with cognition.
2. Associated measures of cognition.

5.3. Example studies of BR

Longitudinally, differences in BR at a point in time could account for the observation that individuals starting at a different level of cognition may show the same rate of age- or disease-related cognitive decline. This could reflect different initial levels (intercepts) due to variation in BR, but similar rates of change (slopes) due to similar depletion of BR. This is distinguished from BM, where slopes would differ as a function of the degree of BM.

BR has also been associated with individual differences in level of cognition given a specific amount of brain change, injury or disease, such as amyloid plaques and neurofibrillary tangles. This association could rely on a threshold model, where a specific amount of depletion of neurobiological capital results disease-related changes. Those who initially have a higher BR can tolerate more depletion before they show symptoms.

6. Conclusion

Here we present a framework that includes well defined operational definitions for 3 concepts: CR, BM and BR. We also propose the term resilience to subsume all of the concepts presented. The operational definitions were carefully designed to be applicable to both human and nonhuman studies.

We believe that the use of a common vocabulary and operational definitions will facilitate research design and communication. The framework also provides a basis for describing how the operational definition of another concept differs from those suggested here.

Our hope for this framework is that a common vocabulary and operational definitions will facilitate even greater progress in understanding the factors that are associated with successful aging and lifelong brain health.

Disclosure statement

None of the authors have actual or potential conflicts of interest to disclose.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neurobiolaging.2022.10.015. This includes: 1. Aknowledgment list 2. descriptions of funded pilot projects and 3,a table that summarizes the projects and how they incorporate the framework presented here.

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Commentary

Lost – and Found – in Translation

Molly V. Wagster[a,*], Jonathan W. King[b]

[a] Division of Neuroscience, National Institute on Aging, Bethesda, MD, USA
[b] Division of Behavioral and Social Research, National Institute on Aging, Bethesda, MD, USA

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In 2017, the National Institute on Aging (NIA) with the support of the Foundation for the National Institutes of Health on behalf of the McKnight Brain Research Foundation, held the Cognitive Aging Summit III. This third Summit was focused on cognitive reserve and resilience, highlighting the increasing importance of these concepts towards understanding age- and pathology-related cognitive change. At the same time, the Summit also highlighted important gaps in our shared understanding of how to characterize terms such as *reserve, resilience*, and *maintenance*; moreover, these gaps appeared to result from a lack of clear and consistent definitions of these and related terms. Disagreements over nomenclature and terminology are hardly new in psychology and neuroscience; indeed, the recognition of Jingle/Jangle fallacies in the measurement literature (Kelley, 1927) has long exposed the obstacles to knowledge advancement that these create. Especially clear at the Summit was that differences in usage of key terms had become serious enough to be more than just a nuisance, impeding (among other things) the ability of researchers using human vs. animal models, cross-sectional vs. longitudinal designs, or neuroimaging vs. neuropsychological approaches to appreciate each other's scientific contributions, much less potentially collaborate. In order to know whether and how a lifestyle, a gene or genes, a personality trait, other factors, or all of the aforementioned confer cognitive reserve, brain maintenance, or resilience to neurodegenerative disease, we need common definitions and a universal language.

When we use the same term to refer to different things (the Jingle Fallacy) or different terms to refer to the same thing (the Jangle Fallacy), fundamental knowledge accumulation and progress predictably grind to a halt. Given the gravity of the inconsistencies in the field, the NIA published a funding opportunity announcement (RFA-AG-18-024, "Collaboratory on Research Definitions for Cognitive Reserve and Resilience to Alzheimer's Disease") to drive the development of operational definitions for the constructs of resilience and reserve, as well as related and often used terms such as compensation, brain maintenance, and even resistance.

In 2018, an award was made to support a unique structure to develop uniform, research-based definitions. Designated as the Collaboratory, the award allowed the investigators to use multiple routes to build definitions and consensus by forming working groups and holding workshops, and to enable the cross-validation of proposed definitions and concepts by supporting small pilot projects.

Besides fostering a common language and thus understanding among researchers for these constructs, the framework developed by the team and presented in this issue of *Neurobiology of Aging* will have far-reaching impact. Understanding, treating, and preventing Alzheimer's disease and Alzheimer's disease related dementias is a national priority for the U.S. If we can harness the knowledge of what confers reserve and resilience, treatments could be targeted to mimic these factors and hopefully prevent or slow disease progression.

The paper in this issue describes the thought processes in which the blue-ribbon Executive Committee for the Collaboratory, aided by many experts around the globe, engaged to reach consensus and provide distilled guidance for the scores of researchers hoping to crack the code on how to gain or maintain successful cognitive performance and brain function with age. As the authors note, these definitions may be subject to revision as we gain more knowledge, but it is the generation of operational definitions like

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* Corresponding author at: Molly V. Wagster, Division of Neuroscience, National Institute on Aging, Gateway Building, Suite 3E400, 7201 Wisconsin Avenue, Bethesda, MD, 20892, USA. Tel.: 301-496-9350; fax: 301-496-1494.
E-mail address: wagsterm@nia.nih.gov (M.V. Wagster).

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these in this framework that will help us more clearly communicate.

Uniformity has its benefits - a common language, operational definitions, and a platform from which to propose alternatives. If we aren't speaking the same language, we will be lost in the translation. This effort insures we can find a path forward.

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Regular article

Extracellular matrix proteoglycans support aged hippocampus networks: a potential cellular-level mechanism of brain reserve

Daniel T. Gray [a], Marc Zempare [b], Natalie Carey [b], Salma Khattab [b], Irina Sinakevitch [b], Lindsay M. De Biase [a], Carol A. Barnes [b,c,*]

[a] Department of Physiology, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA
[b] Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ, USA
[c] Departments of Psychology, Neurology and Neuroscience, University of Arizona, Tucson, AZ, USA

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ABSTRACT

One hallmark of normative brain aging is vast heterogeneity in whether older people succumb to or resist cognitive decline. Resilience describes a brain's capacity to maintain cognition in the face of aging and disease. One factor influencing resilience is brain reserve—the status of neurobiological resources available to support neuronal circuits as dysfunction accumulates. This study uses a cohort of behaviorally characterized adult, middle-aged, and aged rats to test whether neurobiological factors that protect inhibitory neurotransmission and synapse function represent key components of brain reserve. Histochemical analysis of extracellular matrix proteoglycans, which play critical roles in stabilizing synapses and modulating inhibitory neuron excitability, was conducted alongside analyses of lipofuscin-associated autofluorescence. The findings indicate that aging results in lower proteoglycan density and more lipofuscin in CA3. Aged rats with higher proteoglycan density exhibited better performance on the Morris watermaze, whereas lipofuscin abundance was not related to spatial memory. These data suggest that the local environment around neurons may protect against synapse dysfunction or hyperexcitability and could contribute to brain reserve mechanisms.

1. Introduction

One often held misconception of brain aging is that neurodegenerative disease is inevitable; however, only 10%–14% of individuals over 65–70 years of age in the United States are demented (Manly et al., 2022; Plassman et al., 2007). This is not to imply that there are no cognitive changes that occur in normative aging. Rather, the extent of the decline and the domains impacted vary widely across healthy older individuals (e.g., Nyberg et al., 2012; Ryan et al., 2019). These individual differences may be a result of resilience or the capacity of the brain to maintain cognition and function across the lifespan (Stern et al., 2022). While there is still considerable debate regarding the exact nature of resilience, it can be achieved both through active adaptation and by tapping into existing neuronal resources (e.g., Cabeza et al., 2018; Stern et al., 2019, 2022). The factors that facilitate the engagement of brain reserve mechanisms can be either intrinsic to the brain or result from life exposure and can arise through a variety of mechanisms that range from molecular to cellular to network levels.

It has proven relatively challenging to identify robust intrinsic neurobiological features associated with resilience, particularly at cellular and molecular levels of analysis. One major reason for this challenge is that it is difficult to study mechanisms of resilience in animal models. This is because resilience is optimally assessed either through longitudinal study designs that can assess whether life exposure moderates the relationship between brain status and cognition or through cross-sectional studies that require very large sample sizes to appropriately sample the variability in cognitive outcomes necessary to study resilience (Stern et al., 2019, 2022). Despite these challenges, the much wider array of tools available to study the brain at multiple levels of analysis in nonhuman animals compared to humans highlights the importance of developing research aimed at understanding variability in cognitive function in these models of human aging. In rodents and nonhuman primates, one of the neurobiological features that most closely predicts cognitive performance is the number or function of synapses (e.g., Burke and Barnes, 2006; Dumitriu et al., 2010; Hara et al., 2012; Morrison

Abbreviations: CA3, cornu Ammonis 3; CIPL, Corrected Integrated Path Length; NDS, Normal Donkey Serum; OCT, Optimal Cutting Temperature; PBS, Phosphate Buffered Saline; WFA, *wisteria floribunda agglutinin*

* Corresponding author at: Evelyn F. McKnight Brain Institute, University of Arizona, Life Science North, Room 355, Tucson, AZ 85724-5115, USA.
E-mail address: carol@nsma.arizona.edu (C.A. Barnes).

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and Baxter, 2012; Smith et al., 2000). Thus, understanding the details of the variables that impact synapse health is critical to elucidating the biological mechanisms of cognitive resilience in aging. To this end, the present study combines histochemical and image-based analyses of tissue from a relatively large cohort of young adult, middle-aged, and aged rats to investigate potential neurobiological correlates of brain reserve, which is one mechanism by which resilience is thought to be accomplished.

Brain reserve refers to a neurobiological status that allows certain older individuals to evade robust declines in cognition. For a neurobiological factor to be considered brain reserve, it must be associated with some aspect of cognitive function independently of age (Stern et al., 2019, 2022). For example, it has been demonstrated that, regardless of age, rodents with more durable long-term potentiation (LTP) also have more durable memory (Bach et al., 1999; Barnes, 1979; Dieguez and Barea-Rodriguez, 2004). Furthermore, work from rodents, monkeys, and humans has shown that neuronal hyperexcitability of the CA3-dentate gyrus region of the hippocampus emerges with advanced age, most prominently in individuals that exhibit the greatest degree of memory impairment (Spiegel et al., 2013; Thomé et al., 2016; Wilson et al., 2005; Yassa et al., 2011). Immunohistochemical labeling and slice physiology of CA3 neurons indicate that age-associated deficits in inhibitory neurotransmission likely play central roles in this hyperexcitability (Spiegel et al., 2013; Thomé et al., 2016; Tran et al., 2018). These observations predict that neurobiological factors that work to maintain neuronal plasticity and excitatory-inhibitory balances in the hippocampus may represent a form of brain reserve for hippocampus-dependent aspects of cognition.

In this study, we provide evidence that the status of the brain extracellular matrix may represent a form of brain reserve, and we suggest that this is likely accomplished by mediating the relationship between altered inhibitory signaling, CA3/dentate gyrus hyperexcitability (e.g., Small et al., 2002; Thomé et al., 2016; Wilson et al., 2005; Yassa et al., 2011), and memory abilities later in life. The extracellular matrix is a network of proteins and sugars that are secreted from multiple cell types and play critical roles in regulating tissue hydration, ionic balances, and neuronal plasticity (Dityatev et al., 2010). Specialized insoluble aggregations of extracellular matrix proteoglycans called perineuronal nets have garnered significant attention due to their roles in regulating inhibitory neuron function (Sorg et al., 2016). Age-associated reductions in perineuronal nets around inhibitory neurons have been observed in the retrosplenial cortex (Gray et al., 2022; Ueno et al., 2019), which is a region that is critically involved in mnemonic processing and exhibits increased cFos expression (Haberman et al., 2017) and reduced functional connectivity (Ash et al., 2016) in memory-impaired aged rats. While perineuronal net structures in the cortex preferentially aggregate around inhibitory neurons (Brückner et al., 1993; Härtig et al., 1992), the proteoglycans in the hippocampus preferentially accumulate around the somas of CaMKII-expressing excitatory neurons in the pyramidal cell layers of CA2 and CA3 (Lensjø et al., 2017). Whether age impacts hippocampal perineuronal net structures distinctly from those in the cortex has not been assessed. Here, we examine the impact of age on extracellular matrix proteoglycans, specifically in CA3, of behaviorally assessed rats at different points of the lifespan.

2. Materials and methods

2.1. Subjects

A total of 29 adult (6–8 months), 33 middle-aged (15–17 months), and 34 aged (23–25 months) male F344 rats (Harlan Sprague-Dawley, Indianapolis, IN, USA) participated in the study. Rats were housed individually in Plexiglas guinea pig tubs on a reverse 12-hour light-dark cycle and were given free access to food and water. Rats were handled between 5 and 10 minutes per day following their arrival prior to behavioral testing. All protocols described adhered to NIH guidelines and guidelines set by the Animal Care and Use Committee at the University of Arizona (Tucson, AZ).

2.2. Behavioral testing

Rats were tested on the spatial and visually cued versions of the Morris watermaze (Morris, 1984). Rats that were not able to perform the visually cued version of the Morris watermaze were excluded from participation in the study due to the visual demands of this paradigm. The watermaze apparatus consisted of a circular pool with an approximate diameter of 120 cm and a depth of 36 cm. An escape platform was hidden beneath the surface of the water for the spatial version and just above the surface of the water for the cued version (Fig. 1A). Water was made opaque using nontoxic white Crayola paint and maintained at a temperature range between 26°C and 28°C. The apparatus sat in the center of a 2.3 × 2.73 × 2.5 m room that contained several visual stimuli on the walls as distal cues. A chair and a metal board were placed adjacent to the pool as proximal cues.

The full protocol for the Morris watermaze procedure used in this study has been published previously (Barnes et al., 1996). Briefly, the spatial version of the watermaze consisted of 4 sequential days of testing with each rat performing 6 trials per day. For each trial, the rats were given 1 minute to locate the escape platform. If the rat failed to locate the platform after 1 minute, it was guided and placed on the platform for 30 seconds. The procedure for the cued version of the watermaze was identical to the spatial version with the exception that testing was conducted over 2 consecutive days instead of 4. A corrected integrated path length (CIPL) measure was calculated as described in detail elsewhere (Gallagher et al., 1993; Shen and Barnes, 1996; Vorhees and Williams, 2014). Briefly, this measure is derived by calculating an average swimming speed for each animal on each trial as well as the amount of time required to swim to the escape platform in a straight line at that speed. This speed-corrected optimal pathlength is then removed from the record to get the CIPL score. This procedure corrects for the locations of the different start location entry points (some being closer to the platform than others). To evaluate improvement in task performance, a within-subject measure was derived by subtracting the average session 4 CIPL from the average session 1 CIPL (Day 1 – Day 4).

2.3. Histological preparations

Following behavioral testing, all rats were anesthetized with 5% isoflurane and decapitated using a rodent guillotine. The brains were rapidly extracted, flash-frozen in isopentane, cooled over an ethanol bath containing dry ice, and stored at −80°C until cryosectioning. For sectioning, brains were blocked in optical cutting temperature (OCT) compound such that an adult, middle-aged, and aged brain were included on the same slide to reduce technical variability. Sections of 20 µm in thickness were then cut and mounted using a cryostat. Slides were stored at −80°C.

The day before staining, the slides were moved into a −20°C freezer. On the first day of the histological protocol, slides were first removed from the freezer and allowed to thaw for approximately 20 minutes. The tissue was then fixed by submerging slides in 4% paraformaldehyde in phosphate buffer saline (PBS; Sigma-Aldrich, P-5368, 0.01 M, pH 7.4) for 30 minutes. Slides were rinsed in PBS buffer containing 0.01% Triton-X (PBS-TX) and then incubated for 1 hour in a blocking solution consisting of 1% normal donkey serum (NDS; Sigma-Aldrich, D9663) in PBS-TX. A hydrophobic pen was used to

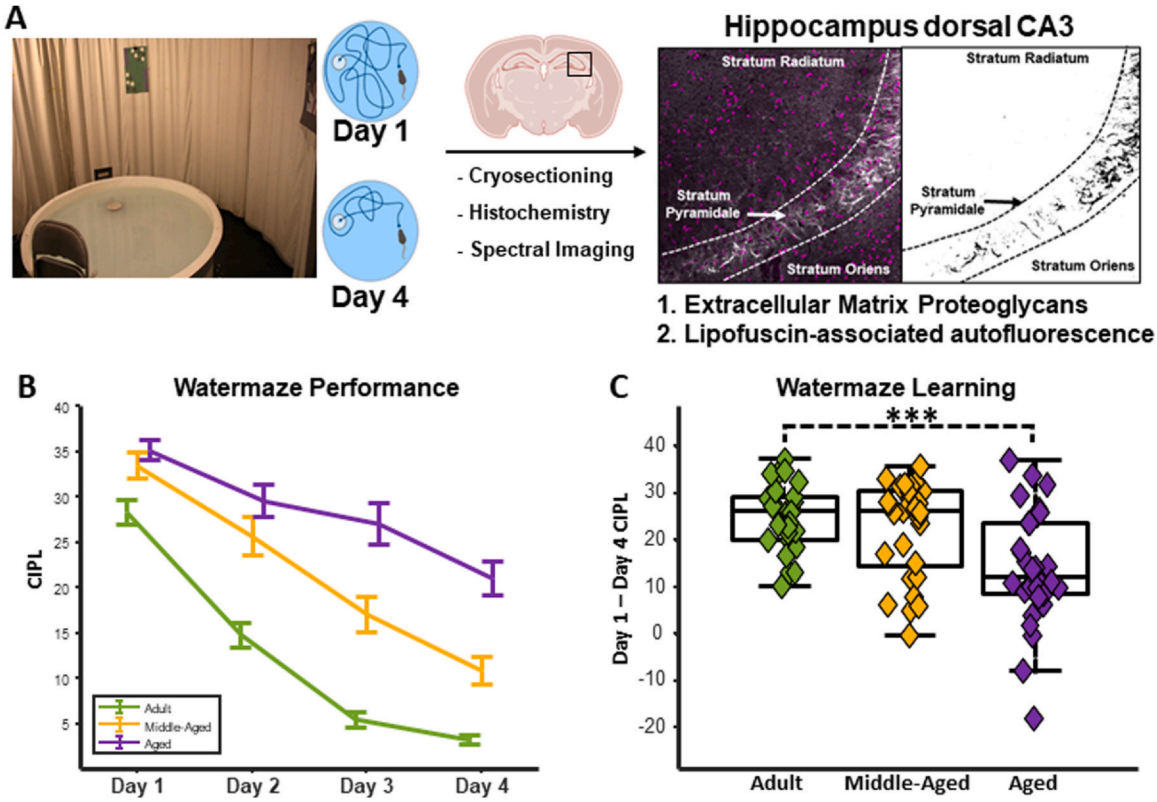

Fig. 1. Experimental design and age comparisons of spatial memory on the Morris watermaze. (A) Image of the Morris watermaze testing environment. The watermaze apparatus consisted of a circular pool with an approximate diameter of 120 cm and a depth of 36 cm and an escape platform hidden beneath the surface of the water for the spatial version and just above the surface of the water for the cued version. Rats underwent 4 sequential days of testing with each rat performing 4 trials per day, and a corrected integrated path length (CIPL) to the escape platform was calculated (see "Methods"). Brains from all animals underwent histological and image-based analyses of extracellular matrix proteoglycan abundance (*wisteria floribunda agglutinin*) and lipofuscin-associated autofluorescence. (B) Average CIPL scores across the 4 days of testing for the adult, middle-aged, and aged rats used in the histochemical analyses. Green represents adult rats, yellow represents middle-aged rats, and purple represents aged rats. Both aged and middle-aged rats exhibited higher CIPL scores than did young across all sessions, and aged rats exhibited higher CIPL scores on the third and fourth days of testing compared to middle-aged rats. (C) The difference measured between day 1 and day 4 of testing. Boxplots denote the middle 50% of the data, and horizontal lines indicate the median of each distribution. Aged rats exhibited a smaller difference, indicating poorer spatial learning. **, $p < 0.01$.

draw a perimeter around all the tissue on the slide, and the blocking solution was pipetted onto the slide. Following incubation in the block solution, the sections were incubated overnight in a solution containing 1% NDS, 0.01% PBS-TX, and biotinylated wisteria floribunda agglutinin (WFA; 1:50; Vector Laboratories, B-1355), which selectively labels N-acetylgalactosamines beta 1 (GalNAc beta 1–3 Gal) residues of glycoproteins within the extracellular matrix (Hilbig et al., 2001). The slides were then washed in PBS-TX (3 × 5 minutes) and incubated in a solution consisting of 1% NDS, PBS-TX, and streptavidin-conjugated Cy5 (peak emission: 670 nm, 1:50; Vector Laboratories, Burlingame, CA, United States; SA-1500). Slides were washed again in PBS (3 × 5 minutes) and coverslipped using 80% glycerol (Vector Laboratories, Burlingame, CA, United States, H-1200-10).

2.4. Confocal imaging and image processing

Brain sections were first imaged with a 40x/1.3 oil objective using a Zeiss LSM 880 inverted confocal microscope to obtain images of native tissue autofluorescence. Image acquisition was performed using a 405-nm laser (Diode 405-30), a 488-nm laser (Argon), and a 633-nm laser (Helium-Neon). All 3 laser lines were used simultaneously in Lambda collection mode using ZEN Black 2.1 imaging software. Lambda collection mode imaging enables the collection of pixel intensity data along the full emission spectrum (410–695 nm) in 32 distinct bins (8.9 nm/bin). For each tissue section, a Z-stack was collected centered on the pyramidal cell layer of the CA3 region of the dorsal hippocampus (Fig. 1A), and these images were fed into a linear unmixing analysis to classify and separate the native tissue autofluorescence from fluorophore fluorescence. The linear unmixing analysis was conducted using ZEN Blue software. The analysis uses a least-squares fit-based algorithm to classify individual pixels into different channels based on their relative contribution to each channel's reference spectrum (Mansfield et al., 2005; Zimmermann, 2005). Unlabeled brain sections were imaged in Lambda mode using the 405-, 488-, and 633-nm lasers to obtain autofluorescence reference spectra, and the reference spectra for each fluorophore were obtained by imaging brain sections with just a single fluorophore. A full description of the linear unmixing procedure was previously published (Pyon et al., 2019). All brain sections were imaged a second time using a 20x objective on a Zeiss Apotome microscope to obtain images of WFA. Again, Z-stacks centered on the CA3 region of the dorsal hippocampus were obtained.

2.5. Image analysis

Image analysis was performed using custom-written macros in Fiji (ImageJ; Schneider et al., 2012) image analysis software. Images of the native tissue autofluorescence and WFA were imported into Fiji, and their contrast was enhanced using the "Enhance Contrast" command. The images were then thresholded using the

"setAutoThreshold" command with the "RenyiEntropy dark" setting with a lower pixel intensity cutoff of 145. The thresholded images were binarized, and the proportion of pixels above the threshold was extracted as an estimate of native autofluorescence abundance and WFA deposition.

2.6. Statistical analyses

Analysis of Morris watermaze performance between age groups was performed using a 2-way analysis of variance (ANOVA) with age as a factor and an α-level of 0.05. *P* values underwent a Bonferroni-Holm correction for post-hoc comparisons. An analysis of WFA deposition and the abundance of autofluorescence were also assessed using a 2-way ANOVA with age as a factor. Individual relationships between anatomical variables and Morris watermaze performance were assessed using a robust regression analysis, also with an α-level of 0.05. All analyses were performed using R Studio statistical analysis software (Boston, MA) or MATLAB (Natick, MA).

3. Results

3.1. Spatial memory deficits increase as a function of age

All rats underwent testing on the spatial version of the Morris watermaze across 4 consecutive sessions. There was a significant effect of the session on the average CIPL scores across sessions, indicating that the animals learned the location of the escape platform (repeated measures AVOVA; $F(3255) = 92.03$; $p < 0.0001$; Fig. 1B). A significant age-by-session interaction was also observed, indicating that older rats exhibit poorer spatial learning across sessions (repeated measures AVOVA; $F(3255) = 11.73$; $p < 0.0001$; Fig. 1B). Post-hoc analyses indicate that middle-aged rats exhibited higher CIPL scores than did young adults across all sessions (*t*-test, Bonferroni-Holm correction; Day 1: $t(53) = -2.65$, $p = 0.01$; Day 2: $t(53) = -4.15$, $p < 0.0001$; Day 3: $t(53) = -5.34$, $p < 0.0001$; Day 4: $t(53) = -3.11$, $p < 0.0001$), as did the aged rats (*t*-test, Bonferroni-Holm correction; Day 1: $t(56) = -4.13$, $p < 0.0001$; Day 2: $t(56) = -6.19$, $p < 0.0001$; Day 3: $t(56) = -8.00$, $p < 0.0001$; Day 4: $t(56) = -8.28$, $p < 0.0001$). Post-hoc comparison also indicates that aged rats exhibited a higher CIPL than did the middle-aged rats on the third and fourth sessions (*t*-test, Bonferroni-Holm correction; Day 1: $t(59) = -0.98$, $p = 0.33$; Day 2: $t(59) = -1.39$, $p = 0.16$; Day 3: $t(59) = -3.29$, $p < 0.01$; Day 4: $t(59) = -4.10$, $p < 0.001$). The difference between day 1 and day 4 CIPL scores was calculated as an estimate of spatial learning, with the older animals showing lower scores (ANOVA; $F(2, 95) = 6.34$, $p = 0.003$; Fig. 1C). Post-hoc tests confirm that aged rats exhibited a smaller difference in performance between day 1 and day 4 compared to young adults (*t*-test; $t(61) = 4.01$, $p = 0.00037$). Although not statistically significant, the same trend was observed when directly comparing middle-aged and aged rats (*t*-test; $t(65) = 2.04$; $p = 0.09$). On the cued version of the watermaze, there was an effect of day of training in all age groups (ANOVA, $F(1, 95) = 72.4$, $p < 0.0001$), indicating that the animals improved performance over days. There was no overall statistically significant difference between age groups (ANOVA, $F(2, 95) = 3.07$, $p = 0.0512$), nor was there an age-by-day interaction (ANOVA, $F(2, 95) = 0.84$, $p = 0.43$).

3.2. Reduced proteoglycan density is associated with spatial memory only in aged rats

An age-associated decrease in WFA deposition was observed (2-way ANOVA; age: $F(1, 84) = 10.187$, $p = 0.002$; Fig. 2B). Post-hoc tests confirm that WFA deposition was lower in aged rats compared to young adults (*t*-test; $t(56) = 3.77$; $p = 0.00079$) but was not different between middle-aged and aged rats (*t*-test; $t(60) = 1.25$; $p = 0.42$), nor between adult and middle-aged rats (*t*-test; $t(54) = 1.73$; $p = 0.17$), although middle-aged rats appeared to show WFA coverage that was intermediate between the young adult and aged rats. When WFA deposition was analyzed with respect to watermaze learning scores, no relationship was observed in the young-adult or middle-aged groups (robust regression; adult: $t(24) = -1.11$, $p = 0.27$; middle-aged: $t(28) = -0.59$, $p = 0.56$; Fig. 2C). Among the aged rats, however, the animals with more WFA in CA3 exhibited better watermaze learning (robust regression; *t*

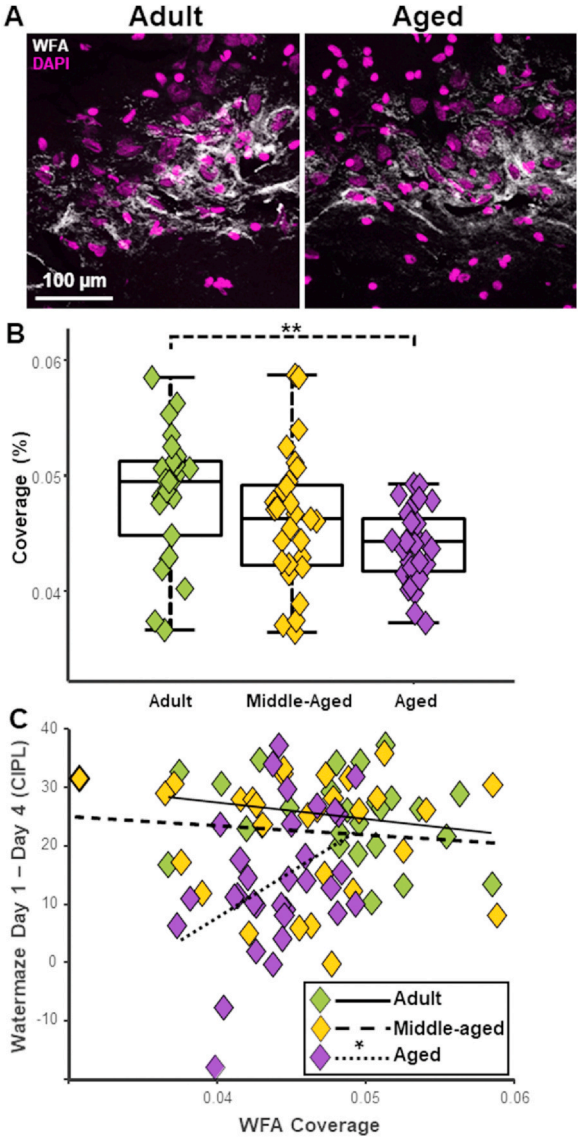

Fig. 2. Aged rats with more extracellular matrix in CA3 exhibited better spatial memory. (A) Representative photomicrograph of *wisteria floribunda agglutinin* (WFA) labeling in the CA3 region of the dorsal hippocampus from a young-adult and aged rat. (B) WFA coverage of dorsal CA3 separated by age. Aged rats exhibited lower WFA coverage than young-adult rats. Boxplots denote the middle 50% of the data, and horizontal lines indicate the median of each distribution. (C) Scatter plot of WFA coverage and Morris watermaze learning scores (Day 1 – Day 4 CIPL difference). There was no significant relationship observed between WFA coverage and CIPL difference scores for the adult and middle-aged rats. Amongst the aged rats, however, the animals with the most WFA coverage showed the best learning on the Morris watermaze. ***, $p < 0.001$.

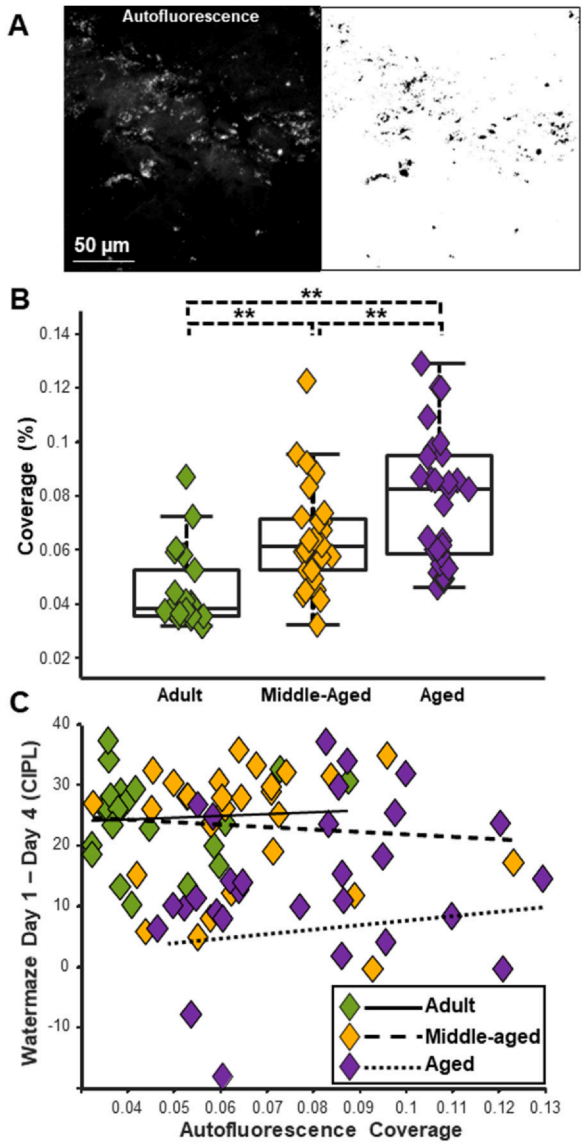

Fig. 3. Lipofuscin increases with age but is not associated with spatial memory. (A) (Left) Representative photomicrograph of lipofuscin-associated autofluorescence in the CA3 region of the dorsal hippocampus. (Right) A threshold image of the same micrograph to show the lipofuscin-associated autofluorescence. (B) Lipofuscin-associated autofluorescent coverage of dorsal CA3 separated by age. Boxplots denote the middle 50% of the data, and horizontal lines indicate the median of each distribution. The older animals exhibited more lipofuscin than did middle-aged or young-adult animals. Middle-aged animals showed more lipofuscin than did young adults. (C) Scatter plot of lipofuscin coverage and Morris watermaze learning scores (Day 1 – Day 4 CIPL difference). There was no significant relationship observed between lipofuscin coverage and CIPL difference scores for any age group. *, $p < 0.05$; ***, $p < 0.001$.

(30) = 2.06; $p = 0.04$; Fig. 2C). These data suggest that extracellular matrix proteoglycans in CA3 represent a biological variable that both changes with advanced age and has an impact on cognitive outcomes.

3.3. Age-associated increases in lipofuscin-associated autofluorescence are not associated with memory

The proportion of a field of view that was covered by lipofuscin-associated autofluorescence (Fig. 3A) was greater in the aged rats compared to young-adult and middle-aged rats (2-way ANOVA; age: $F(1, 75)$: 36.51, $p < 0.0001$; Fig. 3B). Post-hoc tests indicate that tissue from the middle-aged rats contained more lipofuscin compared to young adults (*t*-test; $F(48) = -4.04$, $p = 0.00038$; Fig. 3B), and aged tissue had more lipofuscin than both adult tissue (*t*-test; $F(48) = -5.95$, $p < 0.0001$) and middle-aged tissue (*t*-test; $F(55) = -2.44$, $p = 0.036$). No significant relationships were observed for any age group when lipofuscin coverage was analyzed with respect to watermaze learning scores (robust regression; adult: $t(20) = 0.29$, $p = 0.77$; middle-aged: $t(26) = -0.30$, $p = 0.76$; aged: $t(27) = 0.99$, $p = 0.33$; Fig. 3C). These data indicate that lipofuscin-associated autofluorescence represents a biological variable that changes with advanced age but has no impact on cognitive outcomes.

4. Discussion

The primary finding in this experiment is that aged rats with greater extracellular matrix proteoglycan deposition across the CA3 region of the hippocampus exhibited better spatial memory abilities compared to aged rats with less extracellular matrix protein. Conversely, age-related increases in lipofuscin-associated autofluorescence showed no relationship with spatial memory abilities in any of the age groups. Importantly, the relationship between greater proteoglycan deposition and spatial memory was only observed in aged rats and not in adult or middle-aged rats. This constellation of results fulfills the requirements of the operational definition of brain reserve that was proposed by Stern et al. (2022), which requires measures of aging brain features to be significantly related to cognitive phenotypes expressed in aged animals. In addition, the case for the extracellular matrix being an important component of brain reserve is made stronger by demonstrating the selectivity of this relationship, as age-associated increases in lipofuscin were not related to behavior.

4.1. The extracellular matrix regulates neuronal excitability

Age-associated hyperexcitability in the CA3-dentate gyrus region is thought to arise from a combination of factors, including decreases in inhibitory neuron drive onto excitatory neurons (Spiegel et al., 2013). Proteoglycans in the extracellular matrix play important roles in regulating processes that impact neural network excitability through a variety of different mechanisms. For example, enzymatic degradation of the extracellular matrix results in a significant reduction in inhibitory neuron firing (Balmer, 2016). Proteoglycans likely modulate firing properties due to their strong negative charge, which impacts the local electric field around neurons (Morawski et al., 2015). With age, as proteoglycan deposition decreases, it is possible that the voltage dependence of ion channels is impacted. One hypothesis that emerges from the present data is that, as deficits in inhibitory signaling begin to accumulate in aged brains, the proteoglycans of the extracellular matrix act as a buffer to maintain the network in a healthy physiological state. By extension, aged animals that maintain higher proteoglycan levels may avoid spatial memory impairments. This would be consistent with the idea that the preservation of the extracellular environment may represent a critical aspect of brain reserve.

Enzymatic degradation of extracellular matrix proteoglycans also results in the diffusion of AMPA receptors away from postsynaptic sites, which could alter postsynaptic sensitivity to glutamate release (Frischknecht et al., 2009). At glutamatergic synapses onto inhibitory neurons, the extracellular matrix stabilizes interactions between AMPA receptors and secreted scaffolding proteins such as neuronal pentraxins (Chang et al., 2010). Thus, another hypothesis that emerges from these data is that a breakdown of the hippocampus extracellular matrix and neuronal pentraxins decreases the stability of the glutamatergic drive onto inhibitory neurons. In humans, neuronal pentraxin 2 has been shown to decline in healthy aging and

to be substantially reduced in individuals with Alzheimer's disease. Importantly, in those cases where cognition is within a normal range but the brains show histopathological markers of Alzheimer's disease, neuronal pentraxin 2 is at age-matched control levels (Soldan et al., 2019; Xiao et al., 2017). These authors suggest that this protein protects cognitive function by maintaining a normal excitatory-inhibitory balance in these neural circuits.

4.2. The extracellular matrix regulates synapse function

With age, hippocampal neurons become susceptible to alterations in plasticity by becoming less able to maintain LTP (Bach et al., 1999; Barnes, 1979), more prone to long-term depression (Norris et al., 1996), and LTP reversal (Burke and Barnes, 2006; Norris et al., 1996). In addition to its role in regulating network excitability patterns that impact thresholds for the induction of different forms of plasticity, the extracellular matrix is also positioned to regulate mechanisms of structural synapse plasticity (Dityatev et al., 2010; Nguyen et al., 2020; Sorg et al., 2016). In the adult brain, extracellular matrix structures are thought to inhibit structural plasticity because they emerge toward the end of developmental critical periods and because genetic depletion of critical proteoglycans reinstates these critical periods (Lensjø et al., 2017; Pizzorusso et al., 2002, 2006). Furthermore, it has been shown that the release of matrix metalloproteinases and other degradative enzymes that target the extracellular matrix is necessary for experience-dependent plasticity (Nguyen et al., 2020; Wlodarczyk et al., 2011). Thus, in the adult brain, one function of the extracellular matrix might be to maintain a plasticity threshold that allows neuronal circuits to separate relevant from interfering stimuli. This would fit with the idea that one feature of brain reserve is the ability to preserve homeostatic balance within cells, which serves to optimize circuit function, thereby facilitating higher levels of cognition.

4.3. Extracellular matrix integrity may represent a form of brain reserve

The present findings indicate that it is the relative lack of change in the aged hippocampus extracellular matrix that provides some of the support necessary to maintain spatial memory in aged rats, consistent with a brain reserve mechanism. It is not possible to determine from the present data, however, whether contributions from cognitive reserve or brain maintenance as operationally defined by Stern et al. (2022) also contribute to our findings. A longitudinal design would be necessary to determine whether these other mechanisms of resilience were at play. For example, if the preserved extracellular matrix structure was a result of active adaptation to life-course exposures resulting in better-than-expected cognitive performance given the degree of brain insults sustained, then this would be consistent with a cognitive reserve mechanism. On the other hand, an absence of age-associated changes in the extracellular matrix over time would be consistent with a brain maintenance mechanism. Future longitudinal study designs in nonhuman models of aging will be necessary for determining which mechanisms beyond brain reserve may be playing a role. This would require extremely large initial cohorts to be examined at different time points across the lifespan. Such a study design should be able to capture the true impact that the extracellular matrix, or any other relevant neurobiological variable, has on cognitive outcomes across time.

Authors contributions

DTG conceptualized the experiment, oversaw imaging data collection, performed statistical analyses, and wrote the manuscript. MZ collected and analyzed behavioral data and revised the manuscript. NC collected and analyzed behavioral data. SK collected imaging and behavioral data. IS performed histochemistry, collected imaging data, and revised the manuscript. LMDB provided imaging resources and revised the manuscript. CAB conceptualized the experiment, oversaw behavioral data collection, and wrote the manuscript.

Verification

This manuscript is original, has not been published, and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose.

Disclosure statement

The authors do not have any conflicts of interest.

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Cognitive Aging Summits

2007– Cognitive Aging Summit I (Washington, DC)

The goals and objectives of the conference were to assess the status of current scientific knowledge in normal aging and changes in cognition associated with the aging process; explore new avenues of potential research within the scientific community that could lead to the development of pharmacological and behavioral interventions; and, ultimately, to improved outcomes for the aging; and raise the level of awareness both within the scientific community and among the public about the importance of this area of research and its tremendous value to society.

- **Lead to the Research Partnership in Cognitive Aging between the National Institute on Aging and the MBRF through the Foundation for the NIH in 2009**

2010—Cognitive Aging Summit II (Washington, DC)

Brought together 350 scientists from diverse disciplines to discuss critical questions in age-related brain and cognitive research and explore future avenues of research. The Summit created tremendous excitement among researchers about building a more collaborative approach toward profiling brain health and cognitive function across the lifespan and developing healthy cognitive aging interventions. The concluding half-day segment of the Summit dealt with the development of clinical trials in which considerations for design and new opportunities were considered and discussed.

- **Produced the sentinel article published in The Journal of Gerontology titled "The other 87%" Authored by Drs. Wagster, King, Resnick and Raab**

2017—Cognitive Aging Summit III (Washington, DC)

The themes for the Summit were cognitive and brain resilience and reserve. Over a day and a half, investigators from around the world delivered talks and discussed some of the most important issues facing the public as we seek to find ways to preserve or even improve cognitive function and brain health as we age.

Conference highlights:

The Summit agenda was organized around six topics centered on resilience and reserve, posed primarily in the form of questions:

1. How do we operationalize brain reserve, cognitive reserve, cognitive resilience, and compensation?
2. What are the threats to successful brain and cognitive aging?
3. What are the earlier life contributions to reserve and resilience?
4. What are the later life contributions to reserve, resilience and compensation?
5. How do we validate approaches that aim to harness reserve to improve the aging brain?
6. Innovative approaches in cognitive aging.

In 2018, a set of scientific papers were published based on the content of each of the six sessions at the Summit as a special section in an issue of *Neurobiology of Aging*.

Cost of 2017 Summit: $197,008 (MBRF contributed $171,399 and NIA contributed $25, 610)

2024—Cognitive Aging IV (Bethesda, MD)

The Cognitive Aging Summit IV was held in Bethesda, MD on March 20-21, 2024. The Summit was convened by the National Institute on Aging and made possible by the McKnight Brain Research Foundation through a generous grant to the Foundation for the National Institutes of Health. This fourth Summit was devoted to scientific presentations and discussion of age-related brain and cognitive change,

with a particular focus on individual differences and the development of personalized approaches to the remediation of decline and the maintenance of brain health.

The program content and video-recordings of the Summit can be viewed by clicking on the link below.

https://www.nia.nih.gov/research/dn/cognitive-aging-summit-iv

Cost of 2024 Summit: $335,348 (MBRF contributed $313,573 and NIA contributed $21,774)

William G. Luttge Lectureship in Neuroscience*

2012—MBRF established a lectureship established honoring the Founding Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida

- Lectureship value--$250,000 (See Current Financial statement attached)
- Spendable Fund--$50,000 for immediate inauguration of the Lectureship
- Seventh lectureship was held on March 6, 2019
- Eighth lectureship scheduled for March 2020 was cancelled because of the
- Virtual Lectureship were held monthly throughout the Pandemic.
- Lectureship resumed on February 23, 2023, with Joshua A. Gordon, M.D., Ph.D., director of the National Institute of Mental Health, delivering the **Eighth** Annual William G. Luttge Lecture in Neuroscience delving into the roles of genetics, neural circuits and computational approaches in advancing new understanding and treatment of mental illnesses and cognitive Impairment Impact.
- February 2, 2024— Adam Gassaley, MD, PhD. from the University of California at San Francisco presented the **Ninth** Annual William G. Luttge Lectureship in conjunction with the celebration of the 25th Anniversary of William L and Evely F. McKnight Brain Institute of the University of Florida. Dr. Gazzaley's Luttge Lecture centered around his groundbreaking approaches to "experiential medicine" to optimize brain function.

  View on attached link: https://mbi.ufl.edu/2024/02/06/mbi-celebrates-25th-anniversary-with-illuminating-symposium/

  Fund values December 31.2024:

  - Lectureship--$344,257
  - Spendable Fund--$104,954

*Deceased, March 24, 2012

Society for Neuroscience Annual Meeting
McKnight Brain Research Foundation and the McKnight Brain Institutes
Poster Reception

Background:

The Society for Neuroscience is a professional society, for basic scientists and physicians around the world whose research is focused on the study of the brain and nervous system. Founded in 1969, the Society for Neuroscience (SfN) now has nearly 35,000 members in more than 95 countries. Beginning in 1971, SfN's annual meeting regularly attracts more than 30,000 attendees, representing 80 countries; 536 exhibiting companies; and close to 300 journalists.

In 2006, through a gift agreement with the University of Arizona, the MBRF established the Evelyn F. McKnight Chair for Learning and Memory in Aging and the Evelyn F. McKnight Brain Institute (EMBI) at the University of Arizona. Dr. Carol A Branes was named to occupy the endowed chair and to hold the position of director of the EMBI. Dr. Barnes also served as president of the SFN in 2004-2005.

Beginning in 2008, the McKnight Brain Research Foundation began sponsoring a poster reception in conjunction with the annual meeting of the SfN. The Poster Receptions are hosted jointly by the MBRF and the directors of the four McKnight Brain Institutes located at the University of Arizona, the University of Florida (UFL), the University of Miami and the University of Alabama at Birmingham (UAB). An MBRF Trustee usually acts as the in-person host and presents the awards. Approximately 50 posters were summitted featuring research related to cognitive aging and age-related memory loss.

Posters are judged for prize awards by Dr. Molly Wagster and Dr. Jon King from the National Institute on Aging. Cash awards are for the top three posters - $500, $300 and $200 and $100 for each honorable mention award. Each cash prized is awarded with a certificate of the award.

The annual meeting of the SFN and annual poster receptions were interrupted from 2019-2022 due to the Covid Pandemic.

November 11 – 17, 2023, The Society for Neuroscience restored annual meetings again in Washington, DC. and the Poster Receptions were also resumed.

November 12, 2023, Washington, DC--The 13th Annual McKnight Brain Research Foundation Poster Reception was held at the Embassy Suites DC Convention Center. There were approximately 150 guests, along with 67 registered posters and 3 additional posters which were added the night of the event.

October 6, 2024--The 14th Annual McKnight Brain Research Foundation Poster Reception was held at the Hilton Chicago. There were approximately 147 guests. There were 64 registered posters, and 3 additional posters were added the night of the event. Abstracts received prior to the deadline were included in a poster competition. Registered posters included representations from all four McKnight Brain Institutes.

The poster receptions are thought to be very successful in providing young investigators with the opportunity to present and discuss their research findings via the posters to attendees which include scientists, researchers, clinicians, postdoctoral fellows, graduate, and undergraduate students. Prominent scientists from the National Institutes of Aging as well as neuroscientists at different stages of their careers interested in investigating age-related memory loss are also in attendance.

The average cost for the annual Poster Receptions is $25,000.

MBRF Contact Information
February 2025

Officers

Michael Dockery, MD, Chair
9848 North Tryon St.
Suite 100
Charlotte, NC 28262
mike.dockery@orthocarolina.com
704-651-1887 – cell

Madhav Thambisetty, MD, PhD, Vice Chair
3850 Gray Rock Drive
Ellicott City, MD 21042
madhavtr71@gmail.com
443-852-7607 – cell

Trustees

Patricia A. Boyle, PhD
Professor, Departments of Behavioral Sciences and Psychology
Rush Alzheimer's Disease Center
1750 West Harrison, St, Suite 1000
Chicago, IL 60612
paboyle@gmail.com
312-942-8749

John E. Brady, MD
207 River Road
Newport News, VA 23601
Thevillagedoctor1@gmail.com
757-223-0124

Sharon A. Brangman, MD, FACP, AGSF
203 Old Lyme Road
Syracuse, NY 13224
Biomedical Sciences
BrangmaS@upstate.edu
315-436-0177
Anne Lutz
LutzA@upstate.edu
315-464-5157

Allison Brashear, MD, MBA
Vice President of Health Sciences and Dean of the Jacob School of Medicine and University of Buffalo
955 Main Street, Room 6190
Buffalo, NY 14203-1121
brashear@buffalo.edu
336-770-8122 - cell
Jennifer Markee
Ambrose3@buffalo.edu
716-829-2716

Roy H. Hamilton, MD, MS, FAAN, FANA, FCPP
1012 Fitzwater Street
Philadelphia, PA 19147
215-779-1603
roy.hamilton@pennmedicine.upenn.edu

Sue Pekarske, MD
1281 East Calle de la Cabra
Tucson, AZ 85718
slpekarske@me.com
520-544-3846 – cell

Corporate Trustee

Melanie Cianciotto
Client Manager/Truist
333 S. Garland Ave., 17th Floor
Orlando, FL 32801
melanie.cianciotto@truist.com
321-228-6578 – cell

Chief Executive Officer

Alice H. Luo Clayton, Ph.D.
4 Worchester Lane
Princeton Junction, NJ
08550
aclayton@mcknightbrain.org

McKnight Brain Institutes (MBIs)
Contacts
February 2025

University of Arizona

Carol Barnes, PhD
Director
carol@nsma.arizona.edu

Lee Ryan, PhD
Associate Director
ryant@arizona.edu

University of Alabama at Birmingham

Ron Lazar, PhD, FAHA, FAAN
Director
rmlazar@uabmc.edu

Kristina Visscher, PhD
Associate Director
kmv@ueb.edu

University of Florida

Jennifer Bizon, PhD
Director
bizonj@ufl.edu

Steven T. DeKosky, MD
Deputy Director
steven.dekosky@neurology.ufl.edu

Jada Lewis, PhD
Deputy Director
jada.lewis@ufl.edu

Gordon Mitchell, PhD
Deputy Director
gsmitche@phhp.ufl.edu

University of Miami

Tatjana Rundek, MD, PhD
Director
trundek@med.miami.edu

Bonnie Levin, Ph.D.
Co-Associate Director
blevin@med.miami.edu

Itsham Ul Haq, M.D.
Co-Associate Director
ihaq@med.miami.edu

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McKnight Brain Research Foundation

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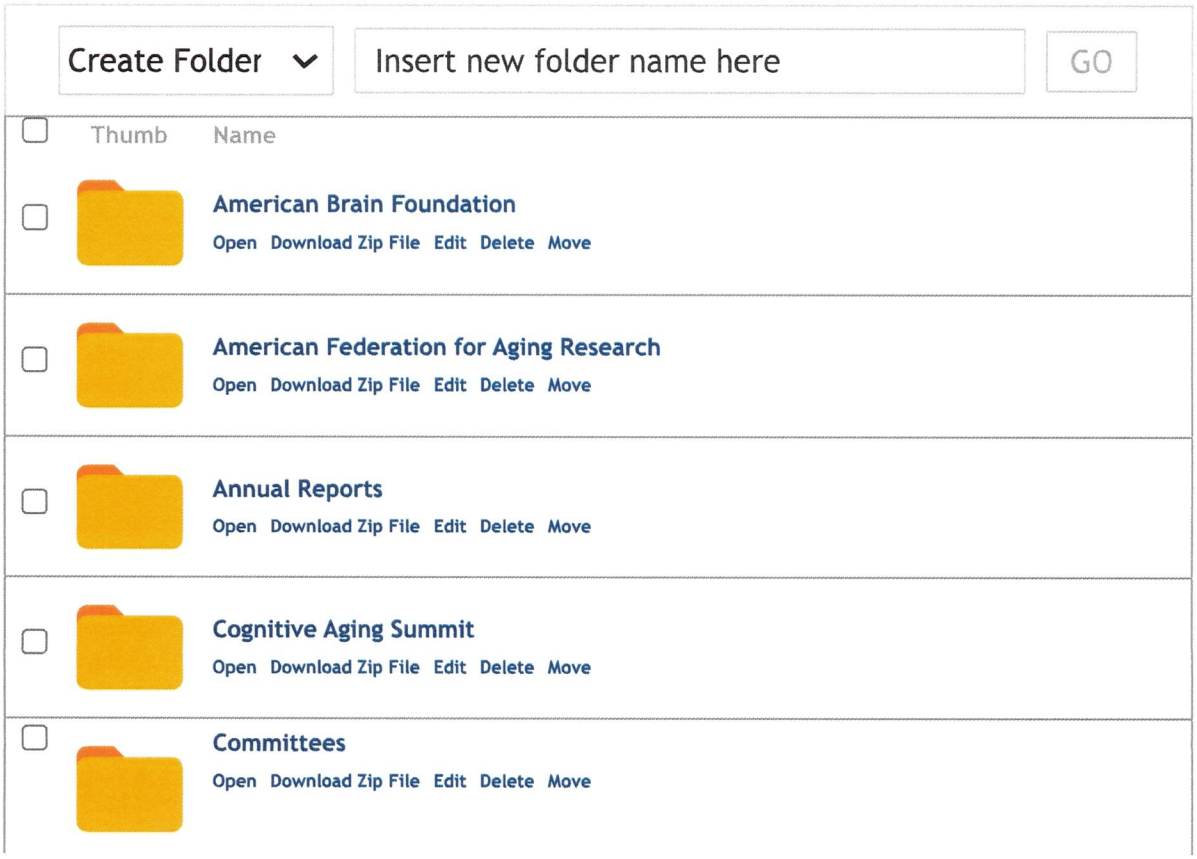

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